
GENETICS AND CELL BIOLOGY

ON FILE™

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GENETICS AND CELL BIOLOGY ON FILE™

The Diagram Group



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Genetics and Cell Biology On File™

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Introduction

Cells were first described in 1665 by Robert Hooke. Since that date, huge strides have been made in understanding the intricate workings of these structures, which are the basic units of all living things. Knowledge of genetics has come a long way since Gregor Mendel formulated, in the mid-1800s, his principles of inheritance. *Genetics and Cell Biology On File™* brings together current knowledge in these key areas of biology. Each section also includes historic discoveries and experiments while selected timelines highlight the milestones in the growth of scientific knowledge.

The first section provides an overview of the major techniques and tools vital to genetics and cell biology. It charts the development of microscopes, which have been fundamental to revealing cellular structures, from early seventeenth-century designs to modern electron microscopes. The vast array of techniques used in the controversial but fascinating field of genetic engineering are surveyed in this section while discussed in detail elsewhere.

Sections 2, 3, and 4 focus on cells. Section 2 introduces readers to the main types of cells, their parts, and their evolution. Section 3 explains in detail the structure and functions of the various parts of the cell and how particular cells carry out their tasks – such as how muscle cells contract and how nerve cells transmit impulses. Section 4 describes the process of cell division: how it normally occurs and what happens when it goes wrong and cancer develops as a result.

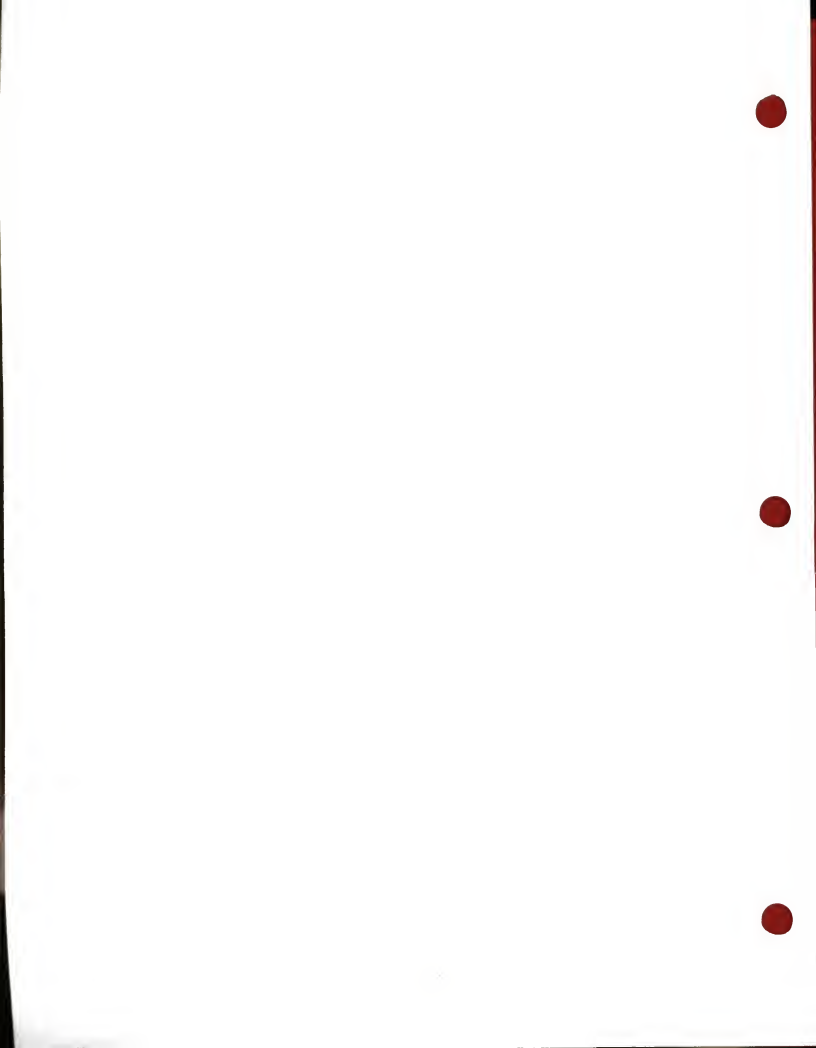
Sections 5, 6, and 7 concentrate on genetics. Section 5 describes the pioneering experiments carried out by scientists such as Mendel and Thomas Hunt Morgan that established the basic principles of inheritance. Section 6 begins with the unraveling of the genetic material itself – DNA – and ends with some of the most up-to-date analytical DNA techniques including gene therapy and DNA fingerprinting. Section 7 looks at theories of evolution and how they have been reevaluated in the light of modern genetics.

Genetics and Cell Biology On File™ is a valuable resource for teachers, students, and those who are simply curious about these areas of biology. It has four major uses:

- as a guide to the way cells function;
- as a guide to how inheritance and evolution operates;
- as a reference resource of images and text for photocopying and including in school and library enquiries; and
- as a basis for examination preparation.

Traditionally books contain narrative text accompanied by illustrations. *Genetics and Cell Biology On File™* is not a book in this sense. Instead, it takes the innovative approach of, wherever possible, letting the illustrations convey information, with text expanding on what is shown visually. Text and illustrations work together to reveal structures, functions, and processes in sharp clarity. Also, unlike in traditional books, the pages of *Genetics and Cell Biology On File™* are plates that work as units on their own. The plates can be approached individually or grouped with other plates on related subjects. In this way, the user can gather a group of plates, from throughout the book, that illuminate many aspects of a particular field of study.

Each topic begins with simple, easy-to-understand principles, providing an overview of relevant structures, processes, or principles and becomes more detailed as it covers the subject in greater depth. Each plate presents its information simply, clearly, and concisely, without assuming any prior knowledge of the subject and avoiding the need to wade through other material. Key facts are presented in a logical and visually interesting way, making them easier to recall. The quality of the artwork is such that it can be reproduced by the most simple photocopier. Care has been taken to avoid the types of tones and textures, so common in many textbooks, that would obscure detail. The text and illustrations have been reviewed and approved by scientists and doctors working in the field.



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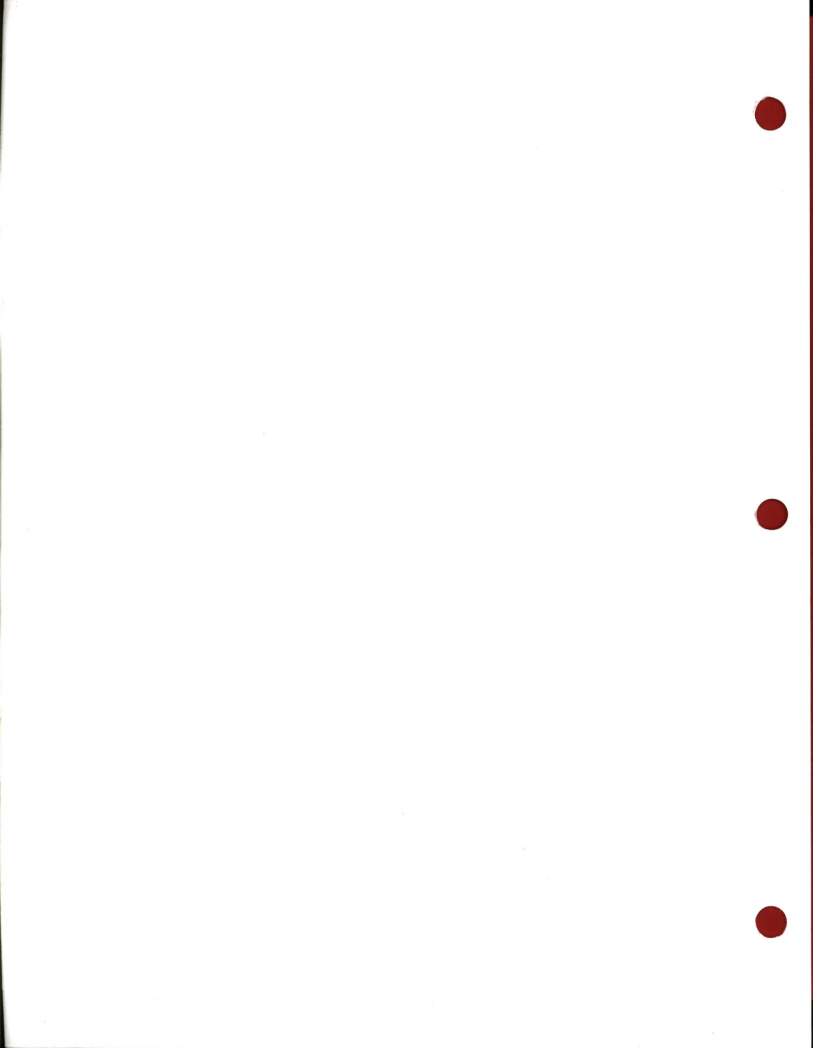
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UNITS OF MEASUREMENT

METRIC UNITS OF LENGTH

1 meter (m) = 100 centimeters (cm)
= 1,000 millimeters (mm)
= 39.4 inches

1 millimeter (mm) = 1/1,000 m
= 1,000 μ m

1 micron (micrometer) (μ m) = 1/100,000 m
= 1/1,000 μ m
= 1,000 nm

1 nanometer (nm) = 1/1,000,000,000 m
= 1/1,000,000 μ m
= 1/1,000 μ m

PREFIXES

- "centi" means one-hundredth
- "milli" means one-thousandth
- "micro" means one-millionth
- "nano" means one-billionth

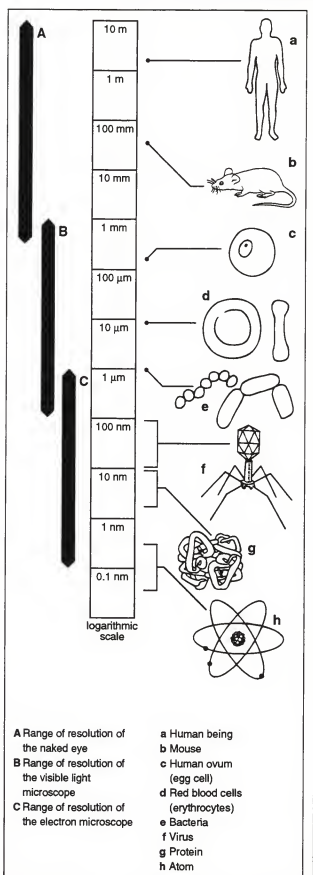
EXPONENTIAL NOTATION

Exponential notation (using powers of ten) is commonly used as a shorthand way of writing very large or very small numbers.

Number	Name	Exponential notation
1,000,000,000	one billion	10^9
1,000,000	one million	10^6
1,000	one thousand	10^3
100	one hundred	10^2
10	ten	10^1
1/10	one tenth	10^{-1}
1/100	one hundredth	10^{-2}
1/1,000	one thousandth	10^{-3}
1/1,000,000	one millionth	10^{-6}
1/1,000,000,000	one billionth	10^{-9}

For example:

1 millimeter (mm) = 10^{-3} m
= 10^3 μ m

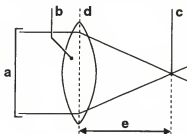


PRINCIPLES OF MICROSCOPY

Optical, or light, microscopes use the properties of lenses to magnify very small objects for study. The double-convex lens with two outwardly-curving sides used in most microscopes produces two kinds of image, real images and virtual images. Although they do not have optical lenses, nonoptical microscopes (for example, electron microscopes) work on similar principles.

FOCAL LENGTHS

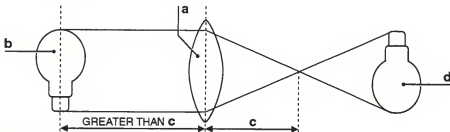
Parallel light rays (a) passing through a double-convex lens (b) are bent inward and converge at point called the focus (c). The distance between the center of a lens (d) and its focus is called one focal length (e). Whether a real or virtual image is formed depends on if the object to be viewed is placed at a greater or lesser distance from the lens than one focal length.



REAL IMAGES

When the distance between the lens (a) and the object (b) is greater than one focal length (c), a real image (d) is formed. A real image:

- may be the same size, smaller, or larger than the object;
- is always inverted and on the opposite side of the lens to the object; and
- as it is formed by actual light rays from the object's surface, it can be projected or used as the object for a second lens.



Magnification of real images

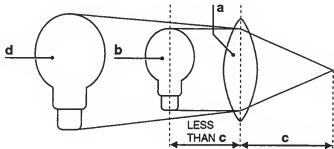
- **Lens curvature** Greater curvature of the lens gives greater magnification.
- **Distance from lens** A larger image can be obtained if the object is between one and two focal lengths from the lens. At two focal lengths from the lens, the image is the same size as the object. At more than two focal lengths, a smaller image is produced.

VIRTUAL IMAGES

When the distance between the lens (a) and the object (b) is less than one focal length (c), a virtual image (d) is formed.

A virtual image:

- appears as if it were more distant and much larger than it actually is;
- is always on the same side of the lens as the object and is not inverted; and
- as no light rays from the object pass through a virtual image, it cannot be projected or used as an object.



Magnification of virtual images

- **Lens curvature** Greater curvature gives greater magnification.
- **Distance from lens** The nearer the object is to the lens, the greater the magnification.

ANTON VAN LEEUWENHOEK'S SIMPLE MICROSCOPE

Microscopy began with Anton van Leeuwenhoek (1632–1723), a Dutch businessman and amateur scientist who ground lenses to use in simple microscopes. He made over 400 such instruments and used them to make the first important observations in cell biology. It was Leeuwenhoek's work that pointed to the existence of a whole new category of living organisms invisible to the naked eye and totally unknown to science.

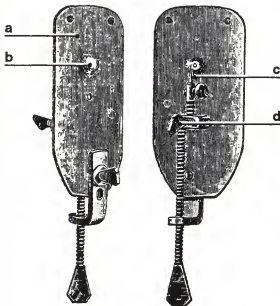
LEEUEWENHOEK'S MICROSCOPES

Principle

A simple microscope uses a double-convex lens with two outward-curving sides to produce an enlarged virtual image (see 1.02) of an object.

How it worked

This particular example consisted of a small, flat, metal plate (a) into which a double-convex lens (b) was fixed. Specimens were placed on a pin (c) that could be adjusted for focusing by means of a screw (d). Leeuwenhoek was a master lens maker and it was the skill with which he ground and polished his lenses that made his observations possible. The greatest magnification he achieved was about 175 times.

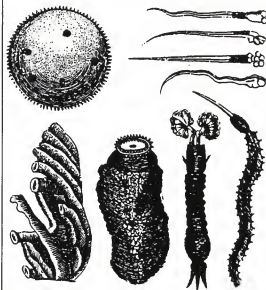


LEEUEWENHOEK'S OBSERVATIONS

In 1672, Leeuwenhoek sent sketches and descriptions of his observations to the Royal Society in London, the foremost scientific organization of the time. This excited much interest and was the start of a long correspondence with the Royal Society. He wrote 165 letters to the society before his death in 1723. Many of these letters were published in the society's journal, *Transactions of the Royal Society*.

Leeuwenhoek was the first to observe unicellular organisms (protists) and, in 1679, human sperm cells. He went on to examine and describe the sperm of birds and many other animals. In 1684, he was the first to describe the red blood cells (erythrocytes) of humans and animals. He also examined the structure of plants, the compound eyes of insects, and the life cycles of fleas, aphids, and ants. He recorded an account of the microscopic life present in scrapings from his own teeth, and made observations of molds.

Some of Leeuwenhoek's drawings of microorganisms. They were based on observations made with his microscopes.



COMPOUND MICROSCOPES 1: IMAGE FORMATION

Compound microscopes had been made by Dutch spectacle maker Zacharias Janssen (1580–1609) and physicist Cornelius Drebbel (1572–1634) some years prior to Anton van Leeuwenhoek's work with simple microscopes (see 1.03). These early compound microscopes had poor quality lenses, however, and could not match the resolving power of Leeuwenhoek's instruments. With improvements in lens making technology, however, the superiority of the compound design became apparent and it was adopted as the standard for biological research.

PRINCIPLE

Compound microscopes use a secondary lens to magnify the image produced by a primary lens.

HOW THE IMAGE IS FORMED

- 1 Light (a) is reflected off a mirror (b) through a condenser lens (c) onto the specimen (d).
- 2 The objective lens (e) – a double-convex lens with two outwardly-curving sides – forms an enlarged real image of the specimen.
- 3 This real image is viewed through an ocular, or eyepiece, lens (f) – also a double-convex lens. This produces the enlarged virtual image that is seen by the eye (g).

Magnification

The final image is enlarged by a factor equal to the magnifying power of the objective and the ocular lens multiplied together. For example, the image from a 40 times objective lens viewed through a 10 times ocular lens will be magnified by a factor of 400 times ($40 \times 10 = 400$).

LIMITATIONS

An optical, or light, microscope cannot resolve images of objects that are smaller than the wavelength of visible light, giving a maximum magnification of about 2,000 times.

ADVANCED COMPOUND MICROSCOPES

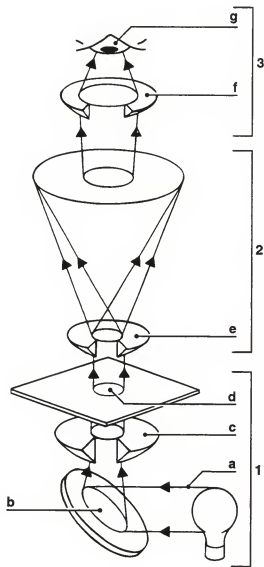
Oil immersion microscopes

Very powerful objective lenses that can magnify an object up to 100 times are used with an oil that fills the space between the lens and the specimen. The optical qualities of the oil allow clearer pictures than if the space is filled with air.

Binocular and stereoscopic microscopes

Some instruments have binocular eyepieces that provide an eyepiece lens for each eye.

Stereoscopic instruments have a set of objective and eyepiece lenses for each eye, providing a three-dimensional image of the specimen.



COMPOUND MICROSCOPES 2: STRUCTURE

ESSENTIAL FEATURES OF A BASIC COMPOUND MICROSCOPE

● **Ocular lens** Compound microscopes have ocular, or eyepiece, lenses (a) with magnification factors of between 10 and 20 times. The ocular lens is mounted in an adjustable lens tube (b).

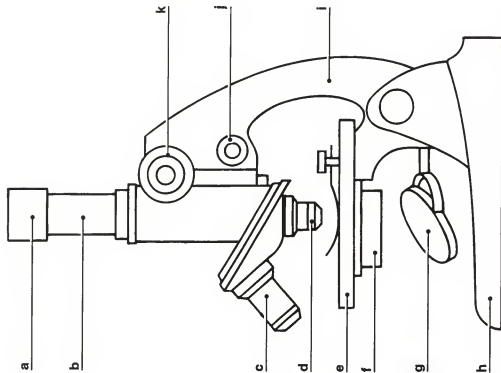
● **Objective lenses** Compound microscopes are commonly fitted with three or four interchangeable objective lenses (c and d), each with a different magnifying factor (usually 4, 10, and 40 times). These lenses are mounted so that they can be easily rotated into place when needed.

● **Viewing stage** Specimens are prepared and mounted on glass slides 76 mm long by 25 mm wide. These slides are held in place with metal clips. The viewing stage (e) has a hole that allows light to shine through the slide from below. Some viewing stages have adjustable mounting brackets that allow the slide to be positioned very accurately.

● **Illumination** Some microscopes have a condenser lens (f), which concentrates light from an adjustable mirror (g) onto the specimen. Artificial or natural light is used.

● **Focus adjustment** To bring an image into focus, the position of the lens tube needs to be adjusted. All compound microscopes have a fine adjustment knob (j), which makes very small movements of the lens tube, and a coarse adjustment knob (k), which makes large movements.

- a Eyepiece/ocular lens
- b Lens tube
- c High-power objective lens
- d Low-power objective lens
- e Viewing stage
- f Condenser lens
- g Mirror
- h Base
- i Arm
- j Fine adjustment knob
- k Coarse adjustment knob



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TRANSMISSION ELECTRON MICROSCOPES AND IMAGE FORMATION

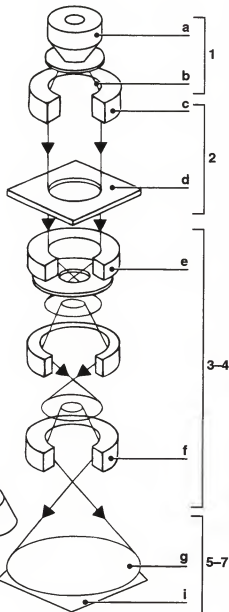
In the past, developments in cell biology were hampered because many cellular structures were too small to be observed using optical (light) microscopes. This was overcome in 1933 when the physicist Ernst Ruska (1906–88) developed a microscope that used shortwave electron beams instead of light to resolve images. This instrument is the transmission electron microscope.

PRINCIPLE

Electron beams are negatively charged, so they can be deflected and focused with electric or magnetic fields. These fields are produced, respectively, by charges on metal plates or by electric currents flowing in deflecting coils. These plates or coils are referred to as electromagnet lenses. All the images formed are real (see 1.02).

HOW THE IMAGE IS FORMED

- 1 An electron gun (a) emits a beam of electrons (b).
The wavelength of the beam can be adjusted to give higher or lower magnification.
- 2 An electromagnetic condenser lens (c) concentrates the electron beam on the specimen (d).
- 3 Some electrons are absorbed or scattered by solid parts of the specimen. The specimen masks part of the electron beam so that the resulting beam casts a "shadow" image of the specimen.
- 4 One or more electromagnetic objective lenses (e) magnify the electron beam image.
- 5 An electromagnetic projector lens (f) focuses the image onto a fluorescent screen (g).
- 6 Electrons strike the fluorescent screen causing a visible shadow image of the specimen to form. Where the electron beam has not been interfered with by the specimen, a bright patch will form. Where electrons have been stopped or scattered, a dark patch will form.
- 7 The image on the fluorescent screen is viewed through a magnifying optical eyepiece (h). It can also be recorded on a photographic plate (i).

**LIMITATIONS**

- A transmission electron microscope cannot easily show surface features or three-dimensional form.
- Since electron beams have wavelengths of less than 0.01 nm, they could theoretically be used to resolve objects down to that size. Imperfections in electromagnetic lenses, however, mean that maximum resolutions are in the order of 0.03 nm.
- The electron beam requires a vacuum to function. Specimens must therefore be dried and living tissue cannot be visualized.

SCANNING ELECTRON MICROSCOPES AND IMAGE FORMATION

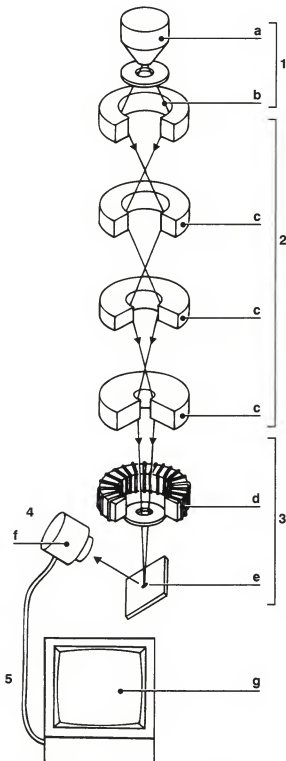
In 1938, shortly after the invention of the transmission electron microscope (see 1.06), physicist Manfred von Ardenne (1907–97) adapted its principles to develop the scanning electron microscope. Ardenne's instrument allowed biologists to directly observe the three-dimensional forms of microorganisms and cell components for the first time.

PRINCIPLE

When electron beams strike a surface they cause electrons on that surface to be displaced and scattered. By scanning a very fine electron beam across the surface of a specimen and measuring the electrons displaced from it, an image of that surface can be built up.

HOW THE IMAGE IS FORMED

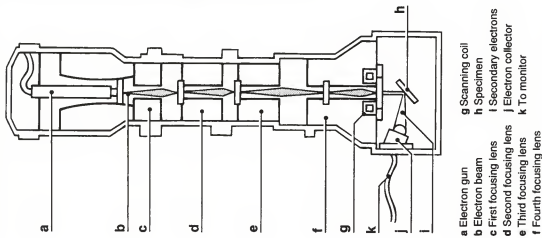
- 1 An electron gun (a) emits a beam of electrons (b). The wavelength of the beam can be adjusted to give higher or lower magnification.
- 2 A series of electromagnetic "lenses" (c) focus the electron beam to a very fine point.
- 3 An electromagnetic coil – the scanning coil (d) – displaces the beam in minute steps so that it scans, in a series of straight lines, across the surface of the specimen (e).
- 4 Electrons displaced from the surface of the specimen are attracted to a positively-charged electrode called the electron collector (f). The displaced electrons cause current changes in the electron collector. These changes are amplified and used to control the intensity of a second electron beam inside a standard cathode-ray (television) tube (g).
- 5 The second electron beam scans across the fluorescent screen of the cathode-ray tube in exact synchronicity with the electron beam scanning across the specimen. An image of the specimen is built up in this way on the screen.

**LIMITATIONS**

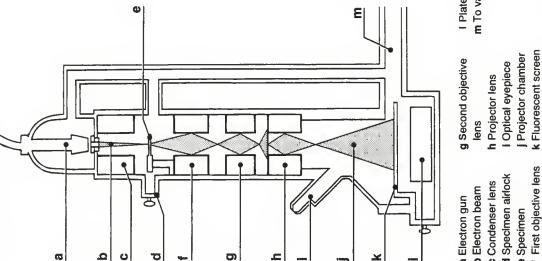
Scanning electron microscopes cannot achieve resolutions as high as transmission electron microscopes, but they do allow three-dimensional images to be formed. They can achieve maximum resolutions in the order of 10 nm.

STRUCTURE OF ELECTRON MICROSCOPES

Simplified section through a basic scanning electron microscope.



Simplified section through a basic transmission electron microscope.



ESSENTIAL FEATURES

- **Vacuum pump** Air must be evacuated from an electron microscope before it is used – air molecules interfere with the passage of electron beams. Some microscopes have an airlock that allows specimens to be changed without repressurizing the whole instrument.
- **Electron gun** The wavelength of the electron beam depends on its speed, which in turn depends on the electrical potential (difference) between the gun's cathode (negative terminal) and anode (positive terminal). The higher the electrical potential, the greater the speed of the beam and the shorter its wavelength. Anode voltages are usually between 20,000 and 1 million volts.
- **Electromagnetic lenses** Transmission electron microscopes often have two or more electromagnetic objective lenses, each with a magnification factor of 100 times. Scanning electron microscopes may have two or more electromagnetic lenses to focus the electron beam.
- **Specimens** For transmission electron microscopes, specimens are prepared as very thin slices (10–100 nm thick). Those for scanning electron microscopes do not need to be sliced. For scanning, some specimens are coated with a very fine layer of metal that improves the flow of displaced electrons.

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CENTRIFUGES

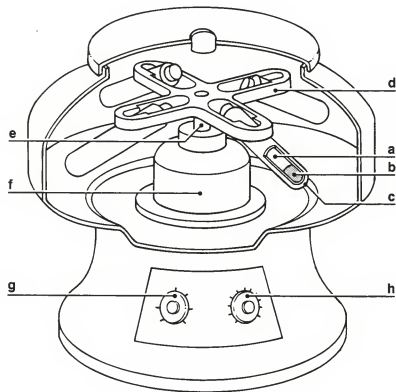
A centrifuge separates materials down to the size of macromolecules (large molecules) either from suspension or solution in liquid.

PRINCIPLE

Particles in suspension will eventually settle out (become a sediment) under the influence of gravity. The more dense the particle, the more quickly it will settle out. A centrifuge speeds up the process of settling out by applying strong centrifugal forces to suspensions. Centrifugal force is the tendency for things to move outward when rotated around a center. Particles of decreasing density can be settled out in turn by applying progressively greater centrifugal force.

HOW IT WORKS

- Strong glass or plastic tubes (a) containing the suspension (b) are inserted into hinged holders (c) in a multiarmed rotor (d).
- This rotor is set on a central spindle (e) driven by an electric motor (f).
- As the spindle rotates, the tubes swing outward into a horizontal position.
- Particles in the suspension collect at the bottom of the glass tubes.

**FEATURES**

- Standard centrifuges are capable of rates of rotation between 800 to 6,000 revolutions per minute (rpm), which generate centrifugal forces of between 1,000 to 100,000 times the force of gravity (g).
- The speed at which a centrifuge rotates can be adjusted (g) over a wide range to allow

particles of different densities to be separated reliably.

- Most centrifuges have a timer (h) that allows the period of rotation to be preset.
- Some centrifuges have a cooler unit so that specimens can be kept cold.

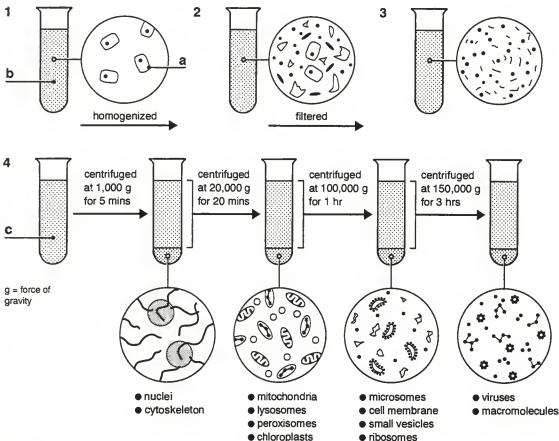
ULTRACENTRIFUGES

Modern high-speed centrifuges rotate on a cushion of air so that no solid parts are in contact to create friction. They are rotated by high-speed jets of compressed air. These ultracentrifuges can achieve rates of up to 80,000 rpm, generating centrifugal forces approaching one million times g. Ultracentrifuges are used to study viruses and other very small particles.

CELL FRACTIONATION

Inside cells are components known as organelles (miniorgans), each of which has a characteristic function, structure, and biochemical composition. In order to study these cell components, they must be isolated through a process known as cell fractionation.

- 1 Specimen cells (a) are suspended in a sucrose (sugar) or saline (salt) solution (b) which closely matches that found inside the cell. The suspension is kept at or near 0 °C (32 °F) to inhibit the action of enzymes (biological catalysts), which would otherwise cause cell components to break down.
- 2 The suspension is processed in a high-speed blender, or tissue homogenizer, to rupture the cell (plasma) membranes – and cell walls if the specimens are plant cells.
- 3 The suspension is filtered to remove undamaged cells.
- 4 The resulting suspension – the cell homogenate (c) – is centrifuged at progressively increasing rates to separate the organelles according to size and density. As each portion of organelles is deposited, the remaining fluid is decanted into another tube and recentrifuged at a higher speed. This is called rate-zonal or differential centrifugation.

**Purity**

The purity of samples is checked by:

- visual examination through an electron microscope, or
- by chemically measuring the concentrations of enzymes known to occur in specific organelles.

Simple centrifugation will not separate cell components with very similar densities. Such components can be separated, however, by using a solution that has a density which increases from the top to the bottom of the tube. During high-speed centrifugation, particles of only slightly differing density will migrate to the level of the solution that matches their own density.

CELL CULTURES

A cell culture is a colony of cells grown in an artificial environment. Cultures are widely used as research tools in biology and as vehicles for the cultivation of viruses for medical purposes. Cell cultures can be regarded as primitive tissues; the terms "cell culture" and "tissue culture" are virtually synonymous. The technique was first demonstrated in the early twentieth century, when chick tissue was successfully grown in glass dishes. Cultures of fibroblasts (immature, connective tissue cells) are now commonplace. Muscle, liver, and some of the more complex epithelial (covering and lining) cells can also be grown. The best source of cells for culture is tissue from fetuses or very young animals because they grow and divide most readily.

**SEPARATING CELLS**

Before they can be cultured, cells from a complex tissue must be separated by breaking down the adhesions between them. This can be done with:

- enzymes (biological catalysts) that dissolve the intercellular junctions and extracellular matrix (material between cells);
- gentle agitation in a liquid; or
- the chelating agent EDTA (ethylene diamine tetraacetic acid). A chelating agent is a chemical that combines with unwanted ions. EDTA removes the calcium ions needed for intercellular adhesion.

**GROWING ANIMAL CELLS IN CULTURE**

Cells will survive and grow only if provided with certain essential nutrients. These nutrients replicate the environment in which the cells would normally grow. They include:

- the essential amino acids (protein building blocks): arginine, histidine, isoleucine, lysine, methionine, phenylalanine, threonine, tryptophan, and valine;
- the nonessential amino acids cysteine, glutamine, and tyrosine, which intact animals can synthesize from specialist cells;
- vitamins;
- glucose (a sugar);
- salts; and
- various blood proteins.

The remaining eight amino acids required for survival can be synthesized by the cultured cells themselves.

**TRANSFORMED CULTURES**

Transformed cultures are cultures of cancer cells. These cells often have far more than the normal number of chromosomes and may be immortal. The best known is the HeLa culture. The original cells of this culture were derived from a tumor in a woman called Henrietta Lacks, who died in the early 1950s. HeLa cells are extremely useful to geneticists and cell biologists because they grow and divide very quickly and continue to do so indefinitely.

CELL HYBRIDIZATION 1

Cell hybridization is the process of fusing two cells from different species together to form hybrid cells. These cells are used to help identify the location of genes on chromosomes. In particular, to locate the defective genes that cause hereditary diseases. Human somatic (body) cells are usually hybridized with mouse or hamster cells.

- 1 Samples of human fibroblasts (immature, 1 connective tissue cells) (a) are taken from an individual who has the particular trait being studied (an inherited disease, for example). Fibroblasts (b) from a normal mouse are also obtained. These cells are mixed together (c).

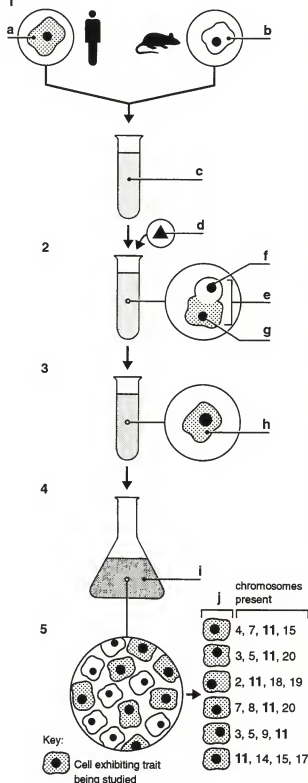
- 2 A fusing agent (d) is added to the cell mixture. This may be a chemical that alters the structure of cells, or an inactive virus that binds cells together. Applying an electric field to a mixture of cells (electrofusion) can have the same result. Fused cells are known as heterokaryons (e). Each has one mouse nucleus (control center) (f) and one human nucleus (g).

- 3 The nuclei of some heterokaryons fuse to form hybridomas (hybrid cells) (h). Hybridomas have one large nucleus, containing complete sets of both the human and mouse chromosomes. Somewhere on the human chromosomes is the gene responsible for the trait, so all of the original hybridomas will exhibit the trait.

- 4 The hybridomas are grown in a cell culture (i). The genetic characteristics of each generation are monitored.

- 5 Hybridomas are unstable. As they undergo mitosis (ordinary cell division), whole human chromosomes or fragments of chromosomes are lost at random. After several generations, the hybridomas (j) that continue to exhibit the trait are extracted and their chromosomes are studied.

When only one particular human chromosome or fragment of chromosome can be found in all the hybridomas that exhibit the trait, then that chromosome can be identified as the location of the responsible gene. In this example, the common chromosome is number 11.



CELL HYBRIDIZATION 2: MONOCLONAL ANTIBODIES

Cell hybridization is also used to produce monoclonal antibodies. This was first achieved in 1975 by Cesar Milstein (born 1927) and Georges Kohler (born 1946) and has allowed great advances in many areas of genetics and cell biology.

An antibody is a protein produced by B-cells (a type of white blood cell). Antibodies can chemically recognize, bind with, and attack specific antigens (substances that provoke an immune response). A monoclonal antibody is produced by a monoclonal (a single, artificially-produced set of identical copies) of a B-cell. The advantage of monoclonal antibodies is that they can be produced in large quantities for an indefinite period – naturally-occurring B-cells die after a few days in culture so there is a limit to how many antibodies they can produce.

PRODUCING MONOCLONAL ANTIBODIES

Mice readily develop a cancer called myeloma. This effects B-cells by causing them to produce antibodies in massive quantities.

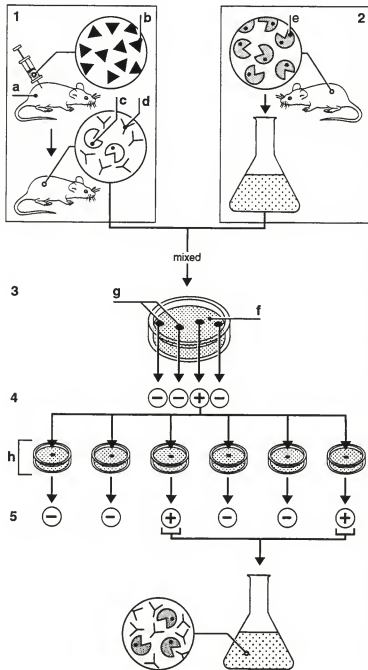
1 A healthy mouse (a) is injected with a particular antigen (b). Its B-cells (c) should then begin making the specific antibodies (d) that target this antigen.

2 Myeloma affected B-cells (e) collected from a cancerous mouse are cultured.

3 The two cell types are mixed together and cultured in a medium (f) that only allows fused (hybridized) cells (g) to grow.

4 The colonies (h) are tested for the specific antibody. Individual cells of those colonies that test positive are separated one at a time and cultured separately to produce clones.

5 These cell lines are tested again for the antibodies. The hybridoma (hybrid cells) that test positive can be used to provide a continuing source of the particular antibody. They have the growth and overproduction characteristics of the myeloma parent, but produce the specific antibody of the healthy B-cell parent.



CHROMATOGRAPHY

Chromatography is a standard method for separating molecules of different sizes from complex mixtures. There are several forms of chromatography used for the analysis of different samples.

PRINCIPLE

When passed through an adsorbent material with either a fluid or gas flow, molecules are attracted by different degrees to the material depending on their size, structure, and chemical properties. This causes the molecules to separate.

Adsorption

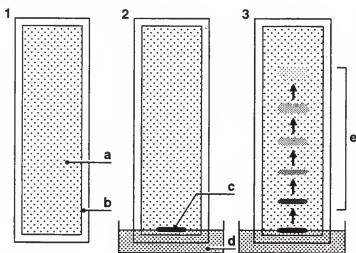
Adsorption differs from absorption. Matter is not distributed throughout an adsorbent material, but collects on its surface. Adsorption is often highly selective, making it useful for chromatography.

Eluants

The eluant is a substance used to move the sample through the adsorptive material. It is often a fluid, but may be a gas.

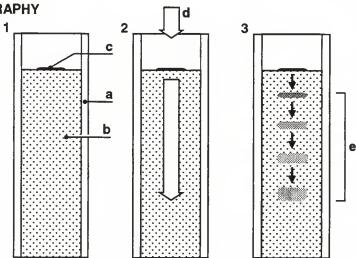
SIMPLE, OR THIN-LAYER, CHROMATOGRAPHY

- 1 A thin layer of adsorbent film (a) is placed on a glass, plastic, or metal plate (b).
- 2 The sample (c) is placed near one edge of the plate. That edge is then brought into contact with the eluant (d).
- 3 The eluant flows upward through the film. Molecules from the sample are adsorbed at different rates, causing them to separate (e) on the plate.



LIQUID-COLUMN CHROMATOGRAPHY

- 1 A tube (a) is filled with adsorbent material (b). The sample (c) is placed on top.
- 2 The eluant (d) is introduced into the top of the column and flows down through the adsorbent material under the influence of gravity.
- 3 Molecules in the sample are adsorbed at different rates; so they travel down the tube at different rates (e).



GAS CHROMATOGRAPHY

This method is used to analyze gases or samples that can easily be converted to gas by heating. Helium is commonly used as the eluant. The sample is passed through a tube containing adsorbent material, as in liquid-column chromatography.

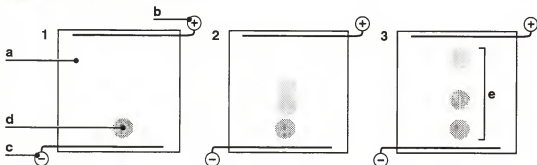
ELECTROPHORESIS 1

Electrophoresis is a widely used technique for separating different types of molecules based on their behavior in an electric field.

PRINCIPLES

- Unlike charges attract; like charges repel.
- Charged particles, such as protein molecules in a sample, are placed at the end of an electric field that has the *same* charge. They will then be *repelled* by the adjacent pole and *attracted* by the opposite pole.
- If those particles are in suspension, they will move toward the attractive pole at different speeds.
- The speed of movement depends on the charge and the size of the molecule: the stronger the charge the higher the speed; the larger the molecule, the slower its speed.

SIMPLE ELECTROPHORESIS



How it works

1 An electrophoretic medium (a) is prepared. This can be an absorbent material soaked in solvent, liquid, or gel. Electrophoretic mediums conduct electricity and allow molecules to move over or through them in an even way.

An anode (positive) terminal (b) is placed in contact with one end of the

electrophoretic medium; a cathode (negative) terminal (c) with the other. The sample (d) is placed at one end.

2-3 When the current is switched on, molecules in the sample begin to move through the electrophoretic medium. Different molecules become separated (e) according to their size and charge.

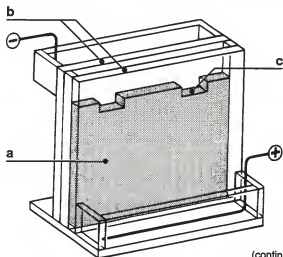
GEL ELECTROPHORESIS

In gel electrophoresis, a porous gel (for example, polyacrylamide or agarose) (a) set between two transparent perspex plates (b) serves as the electrophoretic medium. Regular wells (c) are made in the top of the gel to contain the sample to be analyzed.

Advantages

Electrophoretic gels:

- avoid the problems of convection currents, which can disrupt samples in liquid mediums;
- maintain the separation of components after the current is switched off;
- "sieve" the molecules, enhancing the electrophoretic effect; and
- can be given a pH gradient, allowing isoelectric focusing.



(continued on 1.16)

ELECTROPHORESIS 2

(continued from 1.15)

DNA electrophoresis

- Gel electrophoresis is widely used to determine the length of DNA molecules or fragments. The distance that a sample moves through a gel can be compared to the distance moved by DNA of known length.

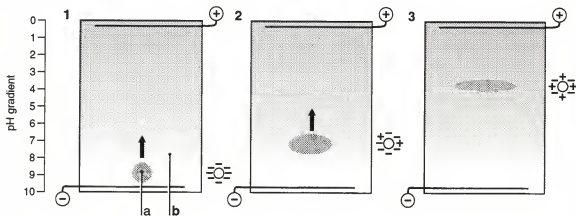
- Pulsed-field electrophoresis (using pulses of current) is used to analyze very large DNA molecules, which tend to break up when in a continuous current.

ISOELECTRIC FOCUSING

Electrophoretic separation of protein molecules can be enhanced by using an electrophoretic medium with a pH gradient.

Principles

- In high pH environments, protein molecules tend to be negatively charged.
- In low pH environments, they tend to be positively charged.
- A protein's isoelectric pH is the level of pH at which it has neither a positive nor negative charge. This varies depending on the chemical structure of the particular protein.

How it works

- 1 A sample (a) is introduced to an electrophoretic medium (b) that has a higher pH level at one end than the other (this is known as a pH gradient).
- 2 The current is switched on and molecules begin to migrate toward the pole of opposite charge.
- 3 As the molecules migrate, they move into different pH environments that alter the strength of their charge. When a molecule

reaches a point where the pH value is such that it is no longer charged, its isoelectric point has been reached. It will no longer be attracted by either pole of the electric field and will stop migrating.

All molecules of the same type in a sample will have the same isoelectric point. They will form a concentration at that point in the pH gradient.

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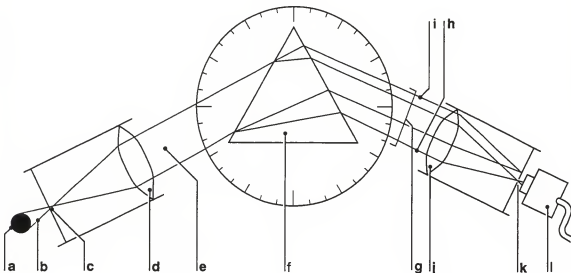
LIGHT SPECTROSCOPY

Isaac Newton (1642–1727) first demonstrated that visible light could be split into a spectrum of colors using a prism. The colors of the spectrum are the light rays of differing wavelengths that comprise visible light. In 1859, Gustav Kirchhoff (1824–87) and Robert Bunsen (1811–99) demonstrated that individual elements and compounds could be identified from their unique light spectra, and established the technique of light spectroscopy (or spectrometry).

PRINCIPLE

- Each substance produces a unique and identifiable spectrum when heated to very high temperatures.
- Substances and their components can

therefore be identified by examining their spectra. This analysis is carried out using a spectrometer – an instrument that displays light as a spectrum.

HOW IT WORKS

- The sample (a) is heated until it is incandescent (emitting visible light).
- Light from the sample (b) enters the spectrometer through a narrow slit (c) and passes through a special lens (d). This lens causes a beam of parallel light rays (e) to form and directs it into the prism (f).
- The prism refracts (bends) the light beam into a spectrum (g). The rays of the beam are refracted by the prism to a greater or lesser degree depending on their wavelength. Violet light (h) has the shortest wavelength and is refracted the most; red light (i) has the longest wavelength and is refracted the least.
- A second lens (j) focuses the light rays of the spectrum so that they pass through a very narrow exit slit (k). Because each ray

emerges from the prism at a different angle, the lens can only focus one at a time. The prism is rotated to allow each ray to be focused through the exit slit in turn. The angle of the prism is recorded each time and used to calculate the wavelength of that ray.

- As each light ray emerges from the exit slit, its intensity (brightness) is registered by a photomultiplier tube (l). This is converted into an electrical value and recorded. With a record of the intensity of each wavelength of light given off by the sample, its exact chemical composition can be determined.

Some spectrometers use a diffraction grating instead of a prism. This is a flat glass sheet with a parallel-grooved surface that diffracts (spreads out) light rays into a spectrum.

MASS SPECTROSCOPY

Mass spectroscopy (or spectrometry) is the process of separating ionized (electrically-charged) atoms or molecules by mass and electrical charge. It enables the identification of elements, molecules, and isotopes (different forms of the same element), and can determine the chemical composition and structure of substances. The first mass spectrometer was built in 1918 by Francis William Aston (1877–1945).

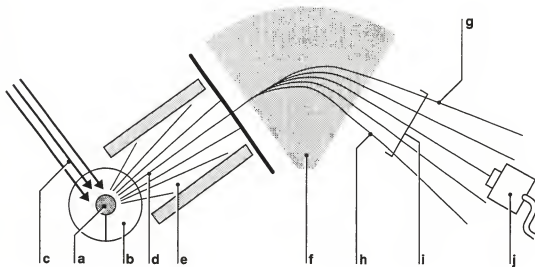
PRINCIPLE

- Mass spectroscopy is based on the same principle as light spectroscopy (see 1.17), except an ion "beam" is created and bent rather than a light beam.
- Ionized molecules are deflected by a magnetic field (the "prism") to a lesser or greater degree depending on their mass and the strength of their electrical charge. The

pattern of this deflection is known as a mass spectrum.

- Each substance has a unique and identifiable mass spectrum. The pattern of deflections from a sample can therefore be used to determine its exact chemical composition.

HOW IT WORKS



- The sample (a) is placed in a vacuum chamber (b) and bombarded with an electron beam (c). This causes ions (ionized molecules) to form.
- A stream of ions (d) is forced from the vacuum chamber by an electric field (e). This field causes the ions to separate according to the strength of their charge. Strongly charged ions are accelerated by the electrical field more quickly than weakly charged ions.
- The accelerated ion beam enters a magnetic field (f). The most strongly charged ions

reach the field first because they have been accelerated the most.

- Ions are deflected by the magnetic field; the heaviest ions (g) are deflected the least, the lightest ions (h) the most. This creates the mass spectrum (i).
- The intensity of the magnetic field is varied very rapidly so that each component of the mass spectrum is directed into an electrical detector (j) in turn. The detector records the ratio of mass to charge of each type of ion in the mass spectrum. A computer interprets the data.

ISOTOPE LABELING AND AUTORADIOGRAPHY

Isotope labeling and autoradiography can be used to trace the movements of substances within cells. The route that a substance takes is known as its biochemical, or metabolic, pathway.

PRINCIPLE

- Many elements occur in more than one form. These alternative forms are called isotopes.
- Isotopes are chemically identical to the element's more common form.
- Some isotopes are radioactive (artificial radioactive isotopes can also be made).
- Molecules into which a radioactive isotope

has been introduced can be tracked as they take part in biochemical processes without the molecules affecting those processes.

- The presence of radioactive isotopes, even in very small quantities, can be detected with a photographic plate. The resulting pictures are called autoradiographs.

HOW IT WORKS

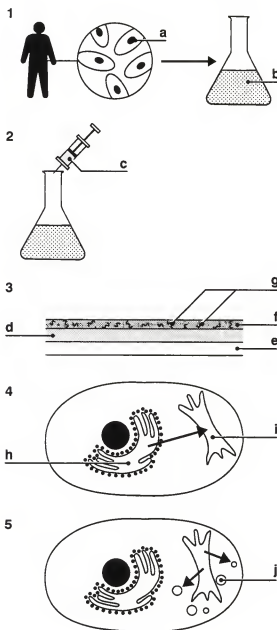
1 In this example, B-cells (a type of white blood cell) (a) from the pancreas are isolated and grown in a cell culture (b).

2 The amino acid leucine, which is used by B-cells to make the hormone (regulatory protein) insulin, is chemically engineered to include the radioactive hydrogen isotope, ^3H . The radioactive leucine (c) is introduced to the cell culture where it is taken up by the B-cells.

3 After 10 minutes, a sample (d) is taken from the culture and placed on a slide (e). This is placed in close proximity to a photographic plate (f). Radiation from the leucine exposes tiny spots (g) on the plate revealing the location of individual leucine molecules.

4 It can be seen that the labeled leucine has moved from the rough endoplasmic reticulum (rough ER) (h) – a type of organelle (miniorgan found in cells) – to the Golgi apparatus (another organelle) (i).

5 After a further 45 minutes, a second photographic plate is used to identify the new location of the leucine. The amino acid can be seen to have moved from the Golgi apparatus to secretory granules (j) in preparation for leaving the cell.



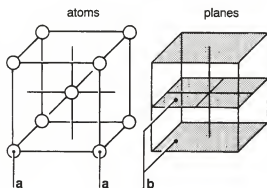
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X-RAY CRYSTALLOGRAPHY

The study of how crystals affect X rays passing through them is called X-ray crystallography.

PRINCIPLE

- The short wavelength of X rays allows them to penetrate substances that do not transmit light.
- The atoms (a) in crystals and crystalline (crystal-like) structures are arranged in planes (b) that have regular spaces between them. X rays passing through the crystal are diffracted (spread out) in a regular pattern by the atoms of these planes, which act as minute mirrors.
- Different crystalline structures produce unique diffraction patterns and these patterns can be used to determine the atomic structure of the substance.

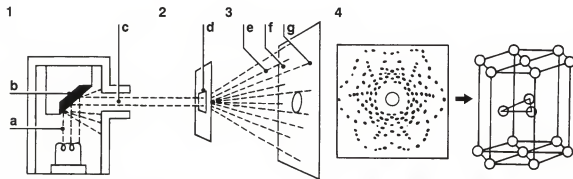


HOW IT WORKS

- 1 Accelerated electrons (a) are aimed at a solid tungsten target (b). When they strike the target, X rays (c) are produced.
- 2 A parallel beam of X rays is directed toward the sample (d).
- 3 The X-ray beam penetrates the sample and is diffracted by its atomic structure. These diffracted X rays (e) are recorded on a photographic plate (f). Where X rays have

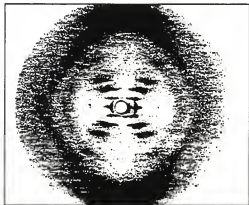
reinforced each other, a spot (g) is exposed. The sample is rotated a few degrees and exposed to another burst of X rays. This is repeated until the sample has been rotated through a full 360°.

- 4 Analysis of the final pattern allows the atomic structure of the sample to be inferred. Powerful computers are used in to analyze complex patterns.



DNA STRUCTURE

In 1953, Francis Crick (born 1916) and James Watson (born 1928) used the work of Maurice Wilkins (born 1916) and Rosalind Franklin (1920–58) to determine the structure of DNA (deoxyribonucleic acid). DNA samples were prepared that were enough like crystals to be able to diffract X rays. This picture, taken by Franklin in 1952, had a very regular pattern that indicated DNA is coiled.



PROTEIN SEQUENCING

Proteins are made up of chains of amino acids. The amino acid sequence of a protein determines its characteristics. This sequence is known as the protein's primary structure. The technique used to determine primary structures is called protein sequencing. It was invented by Frederick Sanger (born 1918). In 1953, Sanger worked out the primary structure of the hormone (regulatory protein) insulin, the first time this had been done for a naturally occurring protein.

1 A pure sample (a) of the protein to be examined is obtained by centrifugation, chromatography, or electrophoresis.

2 Using enzymes (biological catalysts) (b) that are known to split proteins at specific points in their molecular structure, the sample is broken down into its component polypeptides (chains of amino acids) (c).

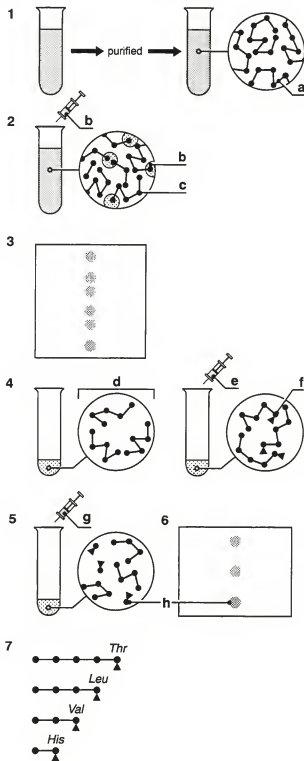
3 The polypeptides are separated according to their size and shape using chromatography.

4 A sample of one kind of polypeptide (d) is treated with the compound dansyl (or dansyl) chloride (e). This forms a strong bond with the last amino acid (f) of each polypeptide. The last amino acid will be the same on each molecule, as they were all "cut" at the same point by the enzymes.

5 The last amino acid is separated from the polypeptide with acid (g). The dansyl chloride-amino acid bonds are not broken by this process.

6 The free dansyl chloride-amino acid pairs (h) are separated from the sample by chromatography. Dansyl chloride can be detected as it is luminous. The amino acid can be identified from its chromatographic behavior. In this case, it is found to be threonine.

7 Dansyl chloride is bonded to the next amino acid in the polypeptide sample. This is separated and identified, in this case, as leucine. The process is repeated until all amino acids in the chain have been identified.



© DIAGRAM

KARYOTYPES 1

A karyotype is a visual representation of all the chromosomes in a cell. Karyotype chromosomes are arranged according to size, shape, and other features.

FEATURES

- Karyotype chromosomes are usually X shaped. This is because chromosomes are most easily identified after they have replicated during cell division.
- In most organisms, every somatic (body) cell has the same karyotype.
- Each organism has its own karyotype. Variations in size, shape, and other aspects make each karyotype unique.
- Karyotypes are species specific. In general, each species has a set number of chromosomes. This is generally called the diploid ($2n$) number. The number of chromosomes in an organism's gametes (sex cells) is usually half the diploid number. This is called the haploid (n) number. In most cases, however, the karyotype is taken from a diploid cell. In some organisms, the number of chromosomes in their gametes is the same as that found elsewhere. These are called haploid organisms.

In the table below, the number of chromosomes in the karyotypes of some species is given.

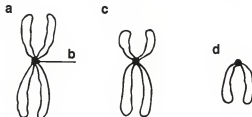
NUMBER OF CHROMOSOMES

Diploid species ($2n$)	
<i>Canis familiaris</i> (dog)	78
<i>Drosophila melanogaster</i> (fruit fly)	8
<i>Felis catus</i> (domestic cat)	38
<i>Homo sapiens</i> (humans)	46
<i>Mus musculus</i> (house mouse)	40
<i>Pisum sativum</i> (garden pea)	14
<i>Zea mays</i> (corn)	20
Haploid species (n)	
<i>Chlamydomonas reinhardtii</i> (unicellular alga)	16
<i>Nerospora crassa</i> (orange bread mold)	7

SORTING CHROMOSOMES BY SHAPE

There are three major shapes used to sort chromosomes within a karyotype:

- a metacentric, in which the chromosome's centromere (constriction) (b) is near the middle;
- c acrocentric, in which the centromere is nearer one end than the other; and
- d telocentric, in which the centromere is right at the end.

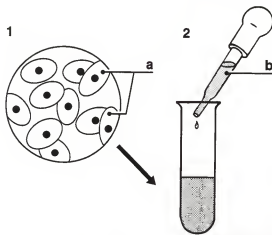


Generally, each species has a set number of these shapes in their karyotypes. The chromosomes of house mice, for example, are all telocentrics.

ISOLATING A KARYOTYPE

In this example, a human karyotype is being prepared.

- 1 Cells (a) are obtained from an individual. White blood cells are often used because they multiply quickly, but any somatic cell will contain a complete set of chromosomes.
- 2 The sample cells are cultured until they enter the metaphase stage of mitosis (ordinary cell division). This is when chromosomes become visible by light microscopy. Chemicals (b) are added that prevent the cells from completing mitosis.



(continued on 1.23)

KARYOTYPES 2

(continued from 1.22)

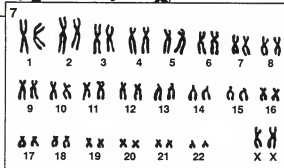
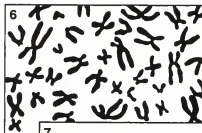
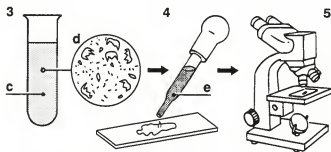
3 The cells are soaked in a salt solution (c) so that they swell and burst (d). This ensures that the chromosomes are spread out.

4 The cell contents are spread on microscope slides and a dye (e) such as Giemsa is added. This stains the chromosomes a dark color.

5 Photographs of the chromosome sets are taken through a high-powered microscope.

6 A photograph that shows the complete set of chromosomes clearly is selected and entered into a computer for analysis.

7 The 46 chromosomes are arranged into 23 homologous (matching) pairs according to their shape and size. The sex chromosomes (X and Y) are identified and separated out. The nonsex chromosomes – the autosomes – are numbered 1 to 22 from largest to smallest. As this example is from a woman, there are two X chromosomes and no Y chromosome. This is the karyotype.

**BANDING KARYOTYPES**

If two chromosomes are very similar in size and shape, it can become difficult to distinguish between them. For this reason, methods that stain certain regions (bands) of the chromosomes with different intensities have been developed.

G banding

Chromosomes are treated with mild heat or certain enzymes (biological catalysts) to partially digest proteins. They are then stained with Giemsa dye to produce the G bands.

Q banding

Quinacrine dye is used to stain regions that are rich in the bases adenine and thymine. Q bands have the same locations as G bands on the chromosomes.



When a banding karyotype is compiled, rod-shaped chromosomes are shown. This is because each half of a replicated (X-shaped) chromosome has identical banding patterns in this respect.

APPLICATIONS

● Karyotypes can be used to identify chromosomal mutations and abnormal numbers of chromosomes.

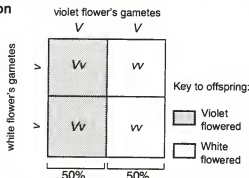
● Banding maps are used by researchers to help identify the location of specific genes on chromosomes.

THE CHI-SQUARE TEST

The chi-square test is a statistical method used to judge the correctness of a theory. Chi-square cannot prove that a hypothesis is correct, only the probability of it being correct.

1 The hypothesis: Mendel's principle of segregation

Gregor Mendel (1822–84) proposed that the two alleles (forms) of a gene separate (segregate) from each other in the formation of gametes (sex cells). In this experiment (a testcross), a violet-flowered plant with the alleles Vv is crossed with a white-flowered plant with the alleles vv . If Mendel's hypothesis is correct, 50% of the offspring are expected to have white flowers and 50% violet flowers.

**2 Observed results of the experiment**

Out of 166 offspring, 85 had violet flowers and 81 had white flowers.

3 Calculating chi-square

The formula for calculating chi-square (χ^2) is: $\chi^2 = \sum \frac{(O-E)^2}{E}$

Where O = observed results and E = expected results. The total of O and the total of E should always be the same. The table below applies this formula to Mendel's results.

Flower color	Observed result (O)	Expected result (E)	$O-E$	$(O-E)^2$	$\frac{(O-E)^2}{E}$
Violet	85	(50% of 166) 83	(85-83) 2	(2 x 2) 4	(4/85) 0.047
White	81	(50% of 166) 83	(81-83) -2	(-2 x -2) 4	(4/83) 0.048
	total 166	total 166			0.095 = χ^2

4 Using chi-square

Chi-square is 0.095 in this case. To understand the significance of this figure, a chi-square table is consulted. These are precalculated tables that list the probabilities of chi-square values occurring by chance for given degrees of freedom.

The degree of freedom is the number of categories that are independent of each other.

Example of part of a chi-square table.

Degree of freedom (df)	Probability			
	0.9	0.5	0.1	0.01
1	0.02	0.46	2.71	3.84
2	0.21	1.39	4.60	5.99
3	0.58	2.37	6.25	7.82

- Probabilities of 0.05 are statistically significant.
- Probabilities of 0.01 are highly statistically significant.
- If chi-square *exceeds* the values listed under these probabilities at the relevant degree of freedom, then the hypothesis is probably incorrect.

In this case, chi-square is lower than these values (*shown in small boxes above*). So it can be assumed that the observed chi-square is not significantly different from the expected chi-square. Therefore, the observed results are consistent with the hypothesis being correct.

For example, as the total number of offspring in our example is 166 and the first class (violet flowers) is 85, then the value of the second class (white flowers) can only be 81. So there is only one independent category.

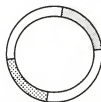
In general, the degree of freedom (df) is equal to the number of classes minus one. In this case, df is $2 - 1 = 1$

GENETIC ENGINEERING 1: OVERVIEW OF TECHNIQUES

Genetic engineering is a broad term that encompasses any deliberate alteration or manipulation of an organism's genes. It includes a wide variety of techniques.

RECOMBINANT DNA

A DNA molecule produced by the combination of two or more fragments of DNA is said to be recombinant. It can occur naturally – during cell division – or can be fashioned by geneticists (see 6.41). Recombining DNA involves a range of molecular manipulations by which lengths of DNA are introduced into the DNA of other cells, or parts of existing DNA are deleted or rearranged. These alterations can be made with great precision, allowing the addition of genes or the modification of particular genes.



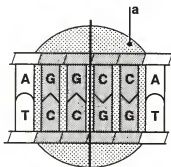
recombinant DNA molecule

RESTRICTION ENZYMES

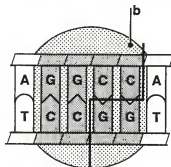
Restriction enzymes (see 6.35) are biological catalysts that "cut" DNA at specific sites. There are hundreds of restriction enzymes, each with a particular recognition site or sites. Some of these enzymes split the DNA clean across between two sets of base pairs; others make a staggered cut so that a few base pairs are separated. This leaves "sticky" ends, comprising unpaired bases that are able to pair up with complementary bases.

Key: | Cutting site
 □ Recognition site

Guanine Cytosine
 Thymine Adenine



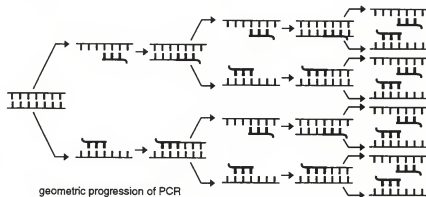
The restriction enzyme *HaeIII* (a) recognizes GGCC and cuts after the second G, cleaving the DNA straight across both strands.



HpaII (b) recognizes CCGG and cuts after the first C. This leaves sticky ends.

POLYMERASE CHAIN REACTION

Genetic engineering demands that once a DNA sequence has been obtained or synthesized, large numbers of copies must be produced. The most efficient way of doing this is by PCR (the polymerase chain reaction) (see 6.40). A tiny sample of DNA can be multiplied a thousand times using an automated PCR process.



geometric progression of PCR

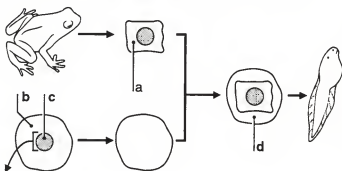
GENETIC ENGINEERING 2: CLONING ORGANISMS

A clone is an identical copy or set of copies of a single ancestor. DNA can be cloned using bacteria (see 6.42). The cloning of a whole organism, however, is a more complex process.

THE FIRST ANIMAL CLONE

In 1968, John Gurdon (born 1933) produced the first animal clone.

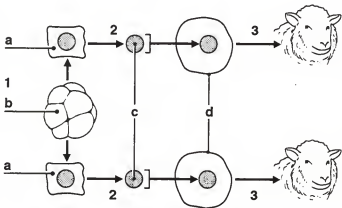
- 1 A single cell (a) from an adult frog was inserted into an egg cell (b) from which the nucleus (c) had been removed.
- 2 This cell (d) grew into a tadpole, but did not reach maturity.



THE FIRST SHEEP CLONES

In 1996, the first sheep clones were cloned from an embryo (an organism in the early stages of development) by a team of scientists led by Ian Wilmut (born 1945).

- 1 Cells (a) were taken from a sheep embryo (b) and cultured.
- 2 The nuclei (c) were transplanted into egg cells (d) from which the nucleus had been removed.
- 3 These cells grew into adult clones called Megan and Morag.



THE FIRST SUCCESSFUL CLONE OF AN ADULT ORGANISM

- Apart from red blood cells and gametes (sex cells) every cell in an organism has the same genome (complete set of genes).
- In the early stages of development, however, most of these genes are chemically "switched off." The only genes kept

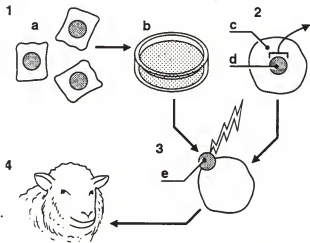
functional are those needed by the particular organ to which the cell belongs.

- The mechanisms that decide which genes are switched on or off remains a mystery. This has been the biggest obstacle to cloning adult organisms successfully.

Dolly the sheep

In 1997, Wilmut and co-workers produced the first successful clone of an adult organism.

- 1 Specialized cells (a) from a sheep's udder were cultivated (b).
- 2 An egg cell (c) was prepared by having its nucleus (d) removed.
- 3 A nucleus (e) from a cultivated udder cell was fused with the egg cell using an electric current. The "new" nucleus responded to the electric current by changing the genes that were switched on.
- 4 Out of 277 attempts, one grew into the adult clone now called Dolly.



Wilmut and his team had managed to produce a whole organism from a cell that had already differentiated into a specialized cell, proving that genes are not irreversibly switched off.

GENETIC ENGINEERING 3: VECTORS

A vector is a piece of DNA that serves as a carrier to insert foreign DNA into an organism. Common vectors include plasmids (circular DNAs separate from the bacterial chromosomes) and viruses (see 6.52). All vectors share certain features:

- one or more sites into which foreign DNA can be inserted;
- the presence of certain markers or features that allow recombinant DNA molecules to be sorted from unrecombined molecules; and
- the ability to replicate in at least one host organism, so that clones can be produced.

SORTING WITH VECTORS

1 The vector

In this example, the vector is a plasmid (a) that has two genes that confer resistance to antibiotics. One gene (b) confers resistance to ampicillin and the other (c) to tetracycline.

2 Inserting the foreign DNA

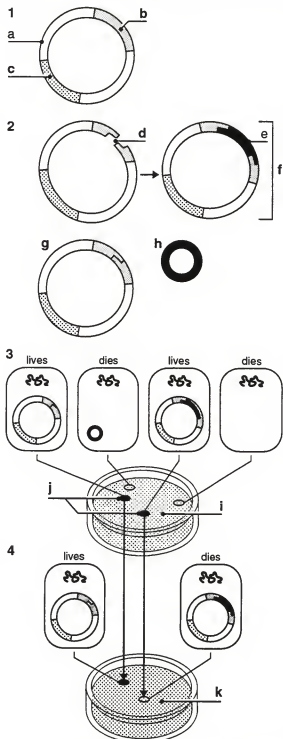
A restriction enzyme is used that cuts the plasmid (d) within the ampicillin-resistance gene. The foreign DNA (e) is inserted at this site to produce recombinant DNA molecules (f). This inactivates the ampicillin-resistance gene. The process of cutting DNA strands and ligating (joining) them with new strands does not happen exactly. Some of the intended vectors ligate without the new DNA (g), and some of the foreign DNA fragments ligate with themselves to form circular molecules (h).

3 Tetracycline selection

This mixture of DNA molecules is mixed with bacteria, some of which take up the DNA. The bacteria are then grown in the presence of tetracycline (i). Only those colonies (j) with the resistance genes will survive. This eliminates those bacteria that did not take up any vectors, including the ones that took up only foreign DNA.

4 Ampicillin screen

To locate the bacteria that took up the vectors, samples are taken from the colonies that survived the tetracycline selection. These are cultured in the presence of ampicillin (k). The recombinant plasmids no longer confer resistance to ampicillin, so their hosts die. The colonies on the tetracycline plate from which these samples came contain the vectors.



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GENETIC ENGINEERING 4: APPLICATIONS AND CONCERNS**APPLICATIONS**

Genetic engineering includes some of the most powerful techniques available to molecular biology. It has very wide applications in medicine, biological research, agriculture, industry, forensic science, and commerce.

**In medicine**

- The production of quantities of biologically important molecules for medical purposes, such as vaccines; human insulin (see 6.45); human growth hormone; and interferons (proteins produced by some eukaryotic cells to combat viral infections).
- As gene therapy, genetic engineering offers potential remedies to treat inherited diseases (see 6.51 and 6.52).
- Using recombinant DNA techniques, it is possible to screen unborn babies for genetic disorders (see 5.32). It may one day be possible to treat babies in the uterus to prevent disease.

**In industry**

- The ability to produce modified microorganisms with specific properties, such as, for example, the ability to break up oil slicks, toxic waste, or garbage.
- The modification of small animals for research purposes (see 6.47).
- The more efficient production of microbes. For example, rennin (an enzyme used to set cheese) is obtained from calves' stomachs. Using genetic engineering technology, however, it can be synthesized more cheaply.

**In agriculture**

- The modification of plants (see 6.46) so as to improve their yield or nutritional value.
- To confer the ability to resist disease or herbicides to crops.
- Genetically altered bacteria have been used on crops to protect them from insects and frost.
- To increase milk production, cattle have been treated with a hormone obtained from genetically engineered bacteria.

CONCERNS

An early concern about genetic engineering was that it would create dangerous bacteria. This fear has largely abated. Many people still query the ethics of manipulating human genes, however. The ability to create transgenic plants and animals leads to the possibility of creating a transgenic human. This is different from the techniques involved in gene therapy, the impacts of which are not passed on to the next generation. Transgenic organisms carry the altered genes in their germ (reproductive cells), and – some would argue – this is equivalent to tampering with evolution. Gene therapy can involve the germ line, but this is currently proscribed.

2. CELL TYPES AND EVOLUTION



TAXONOMY 1

The classification (taxonomy) shown here is based on the five-kingdom system.

CELLULAR ORGANISMS**PROKARYOTES**

Unicellular organisms in which each cell is relatively small and contains no true nucleus (membrane-enclosed control center) or membrane-enclosed organelles (miniorgans).

Kingdom Monera (bacteria and cyanobacteria)

bacterium



cyanobacterium (dividing)

EUKARYOTES

Unicellular and multicellular organisms in which each cell is larger and contains a true nucleus and membrane-enclosed organelles.

Kingdom Protista (protists)

Plantlike and animal-like unicellular eukaryotes.

*Euglena***Kingdom Fungi** (fungi)

Unicellular and multicellular eukaryotes. Fungi obtain their food by absorption from their surroundings.

mushroom

**Kingdom Plantae** (plants)

Multicellular eukaryotes. Most manufacture their own food by photosynthesis using sunlight.

flower

**Kingdom Animalia** (animals)

Multicellular eukaryotes. Most obtain their food by ingestion.

frog

**NONCELLULAR PARTICLES**

Viruses are very simple parasitic particles. They do not have a cellular structure. They depend on cellular organisms for their reproduction.

naked polyhedral virus







enveloped polyhedral virus



complex virus with a tail and a polyhedral head



TAXONOMY 2

CLASSIFYING ORGANISMS	ANIMAL KINGDOM	COMMON FEATURES
<p>The five kingdoms are subdivided into phyla or divisions, classes, orders, families, genera, and finally species. The kingdoms are the largest groups in this hierarchy and the smallest groups are usually the species, though sometimes subspecies (or varieties) exist. Moving down the hierarchy from kingdom to species, the similarities between the members of a group increase, as in the example on the right.</p>	<p>Phylum Chordata</p>  <p>● A notochord (a rodlike structure that supports the body).</p>	<p>● A notochord (a rodlike structure that supports the body).</p>
	<p>Subphylum Vertebrata</p> 	<p>● A notochord, ● which develops into a backbone.</p>
	<p>Class Mammalia</p> 	<p>● A notochord, ● which develops into a backbone; and ● nursing (feeding milk to) their young.</p>
	<p>Order Primates</p> 	<p>● A notochord, ● which develops into a backbone; ● nursing their young; and ● flexible hands and feet.</p>
	<p>Family Hominidae</p>	<p>● A notochord, ● which develops into a backbone; ● nursing their young; ● flexible hands and feet; and ● two legs.</p>
	<p>Genus Homo</p>	<p>● A notochord, ● which develops into a backbone; ● nursing their young; ● flexible hands and feet; ● two legs; and ● habitually walking upright.</p>
	<p>Species Homo sapiens</p>	<p>● A notochord, ● which develops into a backbone; ● nursing their young; ● flexible hands and feet; ● two legs; ● habitually walking upright; and ● a large brain.</p>

PROKARYOTIC AND EUKARYOTIC CELLS 1: AN OVERVIEW

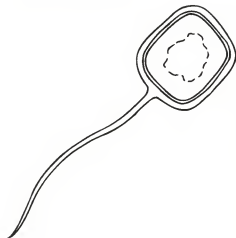
All living things, of whatever species, are composed of cells. All of these cells have certain characteristics in common. Every cell possesses:

- a cell (plasma) membrane;
- DNA (deoxyribonucleic acid) as the genetic (inherited) material;
- proteins;
- the capacity for independent existence;
- the ability to reproduce by division; and
- almost all cells also contain enzymes (biological catalysts).

Despite these similarities, there are important differences between cell types. Since the mid-twentieth century, advances in molecular biology and electron microscopy have made it clear that all known cell types, current and extinct, fall into two major divisions:

- those with a true nucleus (membrane-enclosed control center), and
 - those without a true nucleus.
- These are known, respectively, as eukaryotic and prokaryotic cells.

PROKARYOTIC CELLS



Prokaryotic cells are the unicellular organisms bacteria and cyanobacteria (blue-green algae).

- Prokaryotic cells are small;
- simple in structure;
- lack a true nucleus;
- do not have membrane-enclosed organelles (miniorgans); and
- do not have an extensive cytoskeleton (network of tiny tubes and fibers).
- Cilia (hairlike fronds) and flagella (whiplike extensions of the cell membrane) may be present.
- They usually have a rigid cell wall outside the cell membrane.
- Prokaryotic cells are believed to have evolved before eukaryotic cells.

EUKARYOTIC CELLS



Eukaryotic cells are those found in all cellular organisms other than bacteria and cyanobacteria. These organisms (eukaryotes) comprise unicellular organisms (protists) and the multicellular fungi, plants, and animals.

- Eukaryotic cells are larger than prokaryotic cells;
- have a true nucleus; and
- contain membrane-bound organelles.
- A cytoskeleton is present and might be extensive.
- Some eukaryotic cells also have cilia and flagella.

PROKARYOTIC AND EUKARYOTIC CELLS 2: A COMPARISON

FEATURE	PROKARYOTIC CELLS		EUKARYOTIC CELLS	
	✓ Occurs ✗ Does not occur		PLANT	ANIMAL
Average size		1–10 μm	30–50 μm	10–20 μm
Cell wall		✓ (mainly polysaccharides and protein)	✓ (mainly cellulose)	✗
Cell (plasma) membrane		✓	✓	✓
Nucleus (enclosed by a nuclear envelope)		✗	✓	✓
Nuclear body (without a nuclear envelope)		✓	✗	✗
Chromosomes		<ul style="list-style-type: none"> ✓ single circular chromosome • DNA "naked" – not coated with protein 	<ul style="list-style-type: none"> ✓ many linear chromosomes • DNA combined with histone proteins 	<ul style="list-style-type: none"> ✓ many linear chromosomes • DNA combined with histone proteins
Ribosomes		✓ (smaller)	✓ (larger)	✓ (larger)
Membrane-enclosed organelles:		✗	✓	✓
• centrioles		✗	✓ (in simple plants)	✓
• chloroplasts		✗	✓	✗
• endoplasmic reticulum		✗	✓	✓
• Golgi apparatus		✗	✓	✓
• lysosomes		✗	✓ (some cells)	✓ (many cells)
• mitochondria		✗	✓	✓
• vacuoles		✗	✓ (most cells)	✓ (some cells)
Cytoskeleton:		✗ (entirely or largely absent)	✓	✓
• microfilaments		✗	✓	✓
• microtubules		✗	✓	✓
Cilia and flagella		✓ (when present, of small diameter and simple structure)	✓ (in simple plants)	✓ (some cells)
Cell division		✓ (mostly by binary fission – simple division)	✓ (mitosis and meiosis)	✓ (mitosis and meiosis)
Sexual reproduction		<ul style="list-style-type: none"> • Usually asexual. • Conjugation (transfer of DNA from donor to recipient) occurs. This has been likened to sexual reproduction. 	✓ Meiosis division produces gametes (sex cells), which fuse on fertilization to produce a new organism.	✓ Meiosis division produces gametes (sex cells), which fuse on fertilization to produce a new organism.
Respiration		✓ Can be aerobic (oxygen-using) or anaerobic (respire without oxygen).	✓ The majority are aerobic and need oxygen to live.	✓ The majority are aerobic and need oxygen to live.

EUKARYOTIC CELLS

This is the class of cells from which all living things other than bacteria (prokaryotes) are made. Eukaryotes range from unicellular organisms (protists) to multicellular plants and animals. As a result, they are highly complex and can be very specialized, performing a vast range of tasks. Despite this diversity, all eukaryotic cells share certain features:

- Separation of the genetic (inherited) material – the DNA (deoxyribonucleic acid) – within a nucleus (control center) enclosed by a nuclear envelope.
- The other cell contents are contained in the cytoplasm (semifluid mixture) and, together

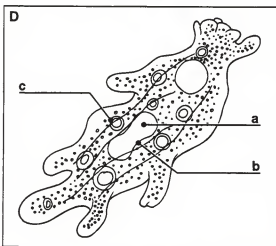
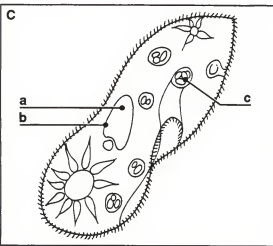
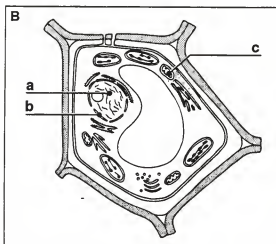
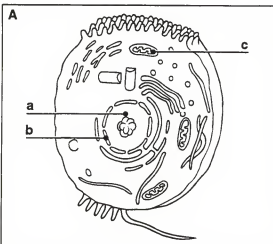
with the nucleus, and are known as organelles (miniorgans). Each organelle performs a specific task or tasks. Some of these structures occur only in certain cell types, while others can be found in many different eukaryotic cells.

- All eukaryotic cells have a cytoskeleton (a network of tiny tubes and fibers) to support their often elaborate internal structures. The cytoskeleton helps to control the shape and locomotion of a cell and the movement of organelles within a cell.

EXAMPLES OF EUKARYOTIC CELLS

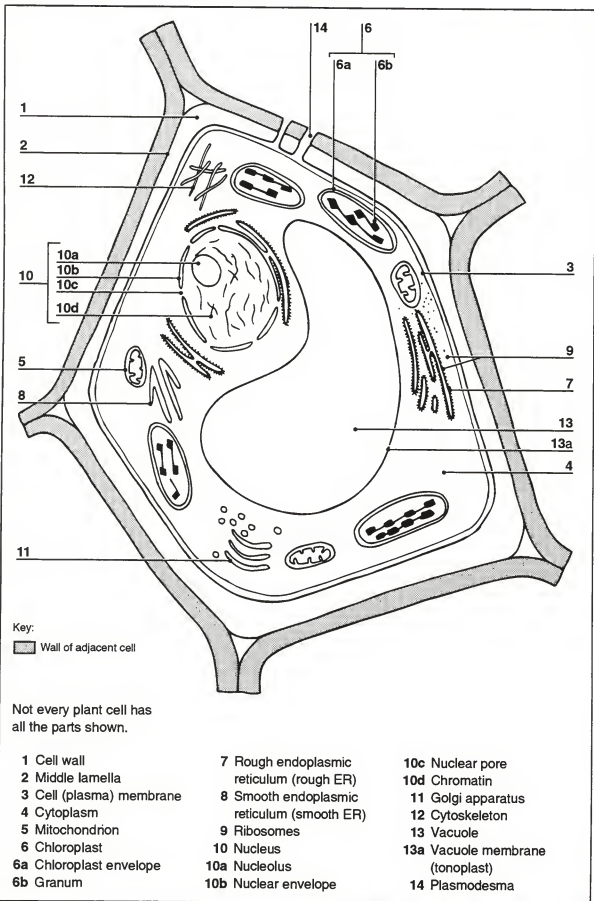
- A** Generalized animal cell
B Generalized plant cell
C Paramecium (a protist)
D Ameba (a protist)

Key:
 a Nucleus
 b Nuclear envelope
 c Organelle



© DIAGRAM

GENERALIZED PLANT CELL 1: STRUCTURE



GENERALIZED PLANT CELL 2: FUNCTION OF PARTS

**CELL WALL**

A cellulose-containing membrane that encloses the cell membrane and:

- forms the external barrier of the cell; and
- enables the transport of substances into and out of the cell.
- The cellulose gives the cell its rigidity and strength, which makes the plant stem stiff.

**MIDDLE LAMELLA**

A cellulose-free layer that holds the cell walls of adjacent cells together.

**CELL (PLASMA) MEMBRANE**

A membrane that encloses the cell's contents and enables transport of substances into and out of the cell.

**CYTOPLASM**

A semifluid mixture that:

- contains the cell's organelles (miniorgans);
- assists in the movement of organelles and transport of substances within the cell;
- provides an environment in which chemical reactions can occur; and
- helps to support and shape the cell.

**MITOCHONDRIA**

Often depicted as threadlike or sausage-shaped organelles, mitochondria are continuously changing shape in living cells. They manufacture the cellular-energy storage molecule, ATP (adenosine triphosphate).

**CHLOROPLASTS**

Large organelles with a double-membrane envelope and elaborate interior membrane systems. The stacks (grana) of the interior membrane contain the green pigment chlorophyll. Chloroplasts enable the plant to carry out photosynthesis to make food.

**ROUGH ER**

A membranous system studded with ribosomes and enclosing a cavity. Rough ER:

- makes the building blocks of the cell membrane, and
- helps to make, store, and deliver proteins.

**SMOOTH ER**

Similar to rough ER, but without any ribosomes. Smooth ER:

- makes fats and cholesterol (a steroid), and
- stores energy.

**RIBOSOMES**

Dense particles composed of RNA (ribonucleic acid) and proteins. Ribosomes help to make proteins.

**NUCLEUS**

A double membrane-enclosed sac containing: chromatin fibers (which comprise DNA – deoxyribonucleic acid – and proteins); nucleoplasm (a gel-like fluid); and the nucleolus. The nucleus:

- controls and regulates the cell's activities;
- transmits genetic (inherited) information during cell division; and
- provides instructions for protein synthesis.
- The nucleolus (a dense sphere made of RNA and proteins) makes ribosomal RNA.

**GOLGI APPARATUS**

A stack of membranous sacs that prepares and delivers proteins for secretion from the cell or for use within the cell.

**CYTOSKELETON**

Tiny tubes and fibers form the cell's "skeleton," which:

- moves organelles within the cell, and
- helps control the shape of the cell.

**VACUOLE**

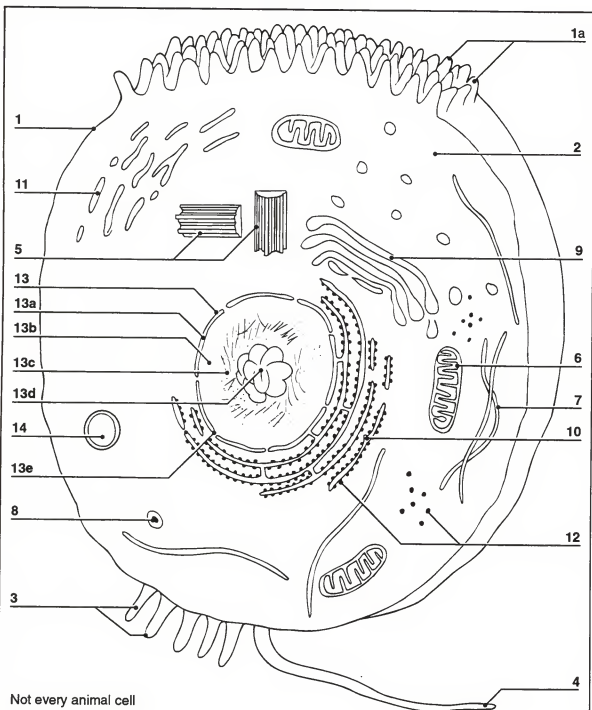
A large, membrane-enclosed, fluid-filled sac that can occupy up to 90% of the cell's volume. The vacuole:

- helps maintain cell shape and osmotic balance (regulation of water content);
- stores sugars, salts, and poisons; and
- pushes the cytoplasm to edge of cell, which aids the intercellular transport of substances.
- The vacuole membrane (tonoplast) controls the movement of substances between the cytoplasm and the vacuole.

**PLASMODESMATA**

Gaps in the cell wall and middle lamella that allow the movement of substances between cells.

GENERALIZED ANIMAL CELL 1: STRUCTURE



Not every animal cell
has all the parts shown.

- 1 Cell (plasma) membrane
- 1a Microvilli
- 2 Cytoplasm
- 3 Cilia
- 4 Flagellum
- 5 Centrioles
- 6 Mitochondrion
- 7 Cytoskeleton

- 8 Peroxisome
- 9 Golgi apparatus
- 10 Rough endoplasmic reticulum (rough ER)
- 11 Smooth endoplasmic reticulum (smooth ER)
- 12 Ribosomes
- 13 Nucleus

- 13a Nuclear envelope
- 13b Nucleoplasm
- 13c Chromatin
- 13d Nucleolus
- 13e Nuclear pore
- 14 Lysosome

GENERALIZED ANIMAL CELL 2: FUNCTION OF PARTS

**CELL (PLASMA) MEMBRANE**

A membrane that encloses the cell's contents and:

- forms the external barrier of the cell;
 - enables the transport of substances into and out of the cell;
 - is involved in intercellular communication; and
 - has receptor sites onto which bacteria, toxins (poisons), or viruses can bind.
- Microvilli (surface folds) increase the absorptive capacity of the cell.

**CYTOPLASM**

A semifluid mixture that:

- contains the cell's organelles (miniorgans);
- assists in the movement of organelles and transport of substances within the cell;
- provides an environment in which chemical reactions can occur; and
- supports and shapes the cell.

**CILIA**

Tiny, hairlike projections that move together in "waves" to propel substances across the cell's surface.

**FLAGELLUM**

A long, whiplike extension of the cell membrane that propels the cell.

**CENTRIOLES**

Organelles like bundles of sticks that appear in pairs. Centrioles:

- form the bases of cilia and flagella, and
- organize the spindle during cell division.

**MITOCHONDRIA**

Often depicted as threadlike or sausage-shaped organelles, mitochondria are continuously

changing shape in living cells. They manufacture the cellular-energy storage molecule, ATP (adenosine triphosphate).

**CYTOSKELETON**

Tiny tubes and fibers form the cell's "skeleton," which:

- is involved in cell motility;
- moves organelles within the cell; and
- helps control the shape of the cell.

**PEROXISOMES**

Membranous sacs containing enzymes (biological catalysts). Peroxisomes detoxify poisons.

**GOLGI APPARATUS**

A stack of membrane sacs close to the nucleus that prepares and delivers proteins for secretion from the cell or for use within the cell.

**ROUGH ER**

A membranous system studded with ribosomes and enclosing a cavity. Rough ER:

- makes the building blocks of the cell membrane, and
- helps to make, store, and deliver proteins.

**SMOOTH ER**

Similar to rough ER, but without any ribosomes. Smooth ER:

- makes fats, cholesterol (a steroid), and some hormones (regulatory chemicals);
- stores energy;
- detoxifies drugs; and
- is involved in muscle cell contraction.

**RIBOSOMES**

Dense particles composed of RNA (ribonucleic acid) and proteins. Ribosomes help to make proteins.

**NUCLEUS**

A double membrane-enclosed sac containing: chromatin fibers (which comprise DNA – deoxyribonucleic acid – and proteins); nucleoplasm (a gel-like fluid); and the nucleolus. The nucleus:



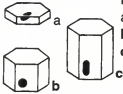





- controls and regulates the cell's activities;
 - transmits genetic (inherited) information during cell division; and
 - provides instructions for protein synthesis.
- The nucleolus (a dense sphere made of RNA and proteins) makes ribosomal RNA.

**LYSOSOMES**

Membranous sacs containing acidic particles. Lysosomes:

- digest substances, and
- destroy harmful, damaged, or useless cells.

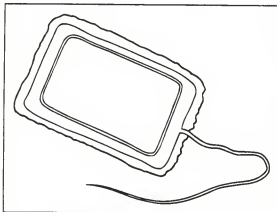
TYPES OF ANIMAL CELLS

CELL TYPE	DESCRIPTION	LOCATION	FUNCTIONS
Adipocytes 	Each contains a droplet of fat that pushes the nucleus and cytoplasm to the edge of the cell.	Deposited under the skin and around the heart and other organs as fat.	<ul style="list-style-type: none"> ● Store energy; ● cushion body parts; and ● provide insulation.
Chondrocytes 	Large and circular.	In cartilage (semirigid connective tissue).	<ul style="list-style-type: none"> ● Maintain cartilage and ● in their immature form (chondroblasts) make cartilage.
Epithelial cells 	There are three main types: a squamous (flat); b cuboidal; and c columnar.	In the coverings and linings of the body.	<ul style="list-style-type: none"> ● Protect, ● absorb, ● secrete, ● filter, and ● allow stretching.
Fibrocytes 	Long, flat, and branching.	In connective tissues.	<ul style="list-style-type: none"> ● Maintain fibers and ● in their immature form (fibroblasts) make fibers.
Leukocytes 	White blood cells of various shapes and sizes; they are larger than red blood cells.	Throughout the body.	Fight and destroy invading germs and bacteria.
Neurons 	Nerve cells with short extensions called dendrites (a) and a single, longer extension called an axon (b).	Throughout the body; in particular, in the brain and spinal cord.	Transmit electrical charges – nerve impulses.
Osteocytes 	Mature, circular bone cells.	In bones.	<ul style="list-style-type: none"> ● Maintain bones and ● in their immature form (osteoblasts) make bones.
Erythrocytes 	Disk-shaped red blood cells that lose their nuclei (control centers) during development.	In the bloodstream.	Transport gases around the body.
There are many other types of animal cells not shown here.			

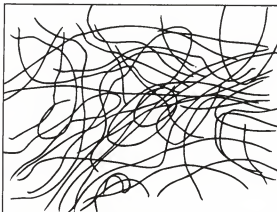
PROKARYOTIC CELLS

Prokaryotic cells are those that do not have a true nucleus (membrane-enclosed control center). Prokaryotes are believed to be the earliest living organisms; they were the only ones until about 1.5 billion years ago. All prokaryotes are bacteria: very small, unicellular organisms, usually between 0.3 to 2.0 μm in diameter. They are present in almost all environments. Although some bacteria are harmful, most are benign and their presence is fundamental to life on Earth.

EXAMPLES OF PROKARYOTIC CELLS



Generalized diagram of a common bacterium (rod-shaped).



Anabaena alga, consisting of long strands of single cells. This is a type of prokaryote called cyanobacteria (blue-green algae).

FEATURES OF PROKARYOTIC CELLS

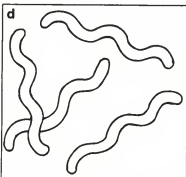
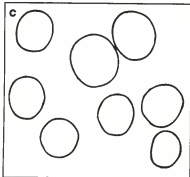
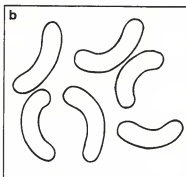
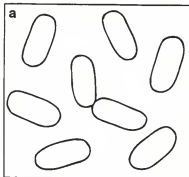
- They are microscopic or ultramicroscopic.
- They often possess a tough outer coat of mucopolysaccharide (a complex of protein and sugars).
- The cell (plasma) membrane allows materials to enter or leave by diffusion.
- Bacteria are capable of rapid binary fission (simple division) with a generation time as short as 20 minutes. Under optimal conditions, prokaryotic cells could produce a population much greater than the human population of the Earth in less than a day.
- They are capable of rapid evolution, thanks to their exponential population growth.
- Prokaryotes can derive nourishment from a wide variety of organic molecules and, in the case of the cyanobacteria, even from atmospheric nitrogen and carbon dioxide.
- In most cases, they are capable of performing many metabolic chemical reactions by virtue of the presence of hundreds of enzymes (biological catalysts).
- Aerobic bacteria need oxygen to grow;
- anaerobic bacteria do not need oxygen but some can tolerate its presence.
- During respiration, prokaryotic cells can pump hydrogen ions out of the cell across their cell membrane. This establishes a gradient, and the movement of hydrogen ions back into the cell is used to generate ATP (adenosine triphosphate). ATP provides the cell with energy.
- They can transfer genetic (inherited) material by various processes, including one that is similar to sexual reproduction.
- In some cases, prokaryotic cells are capable of producing highly-toxic substances that can induce diseases in plants and animals, including humans.
- Cyanobacteria contain gas vacuoles (pockets) that allow the adjustment of buoyancy in water.
- Some contain particles that react to magnetic fields, allowing orientation and movement along the lines of the Earth's magnetic field.

TYPES OF BACTERIA

SHAPE

Bacteria are classified according to their shape:

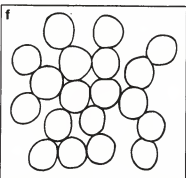
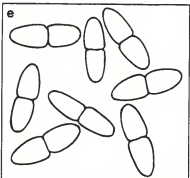
- a** bacilli are rod-shaped bacteria;
- b** vibrios resemble bent rods;
- c** cocci are spherical bacteria; and
- d** spirilla are spiral-shaped bacteria.



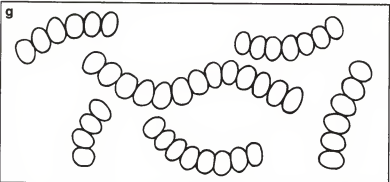
ARRANGEMENT

Various prefixes are also used to denote how two or more bacteria are linked together:

- "diplo-" denotes paired bacteria;
- "staphylo-" denotes clustered bacteria; and
- "strepto-" refers to bacteria in chains.

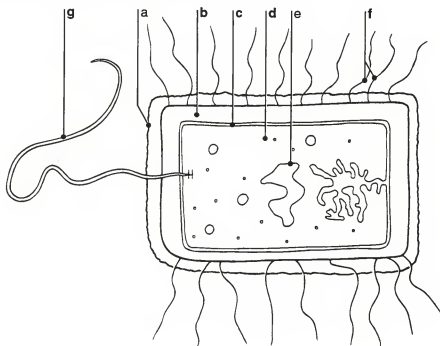


- e** Diplococci
- f** Staphylococci
- g** Streptococci



GENERALIZED BACTERIUM: STRUCTURE AND FUNCTION

Not every bacterium possesses all of the structures shown.



STRUCTURE

FUNCTIONS

a Capsule

A slimy layer that protects the cell from destructive chemicals.

b Cell wall

- The strength of the cell wall allows it to survive in conditions that might otherwise lead to swelling and fatal rupture.
- Bacteria are either Gram-positive or Gram-negative based on whether they stain purple or pink with the Gram test – a method developed by Danish physician Hans Christian Gram (1853–1938). The difference between Gram-positive and Gram-negative bacteria is in the chemistry of their cell walls. The two classes react differently to antibiotics. This is because antibiotics are substances that mainly function by the effect they have on the cell wall.
Gram-positive bacteria are stained deep purple by the Gram test. **Gram-negative bacteria** are stained reddish pink. These bacteria have a more complex, multilayered wall which, due to its components, allows the original stain to be washed out.

c Cell (plasma) membrane

- Provides the site of energy synthesis.
- Pores allow the passage of small food molecules.

d Cytoplasm

Gel-like substance that contains enzymes (biological catalysts), which break down food and build cell parts.

e Nuclear body

An area of genetic (inherited) material: DNA (deoxyribonucleic acid). DNA controls the cell's activities. The nuclear body is not surrounded by a membrane and is therefore not a true nucleus.

f Pili

Allow DNA to be exchanged during conjugation (see 6.24)

g Flagellum

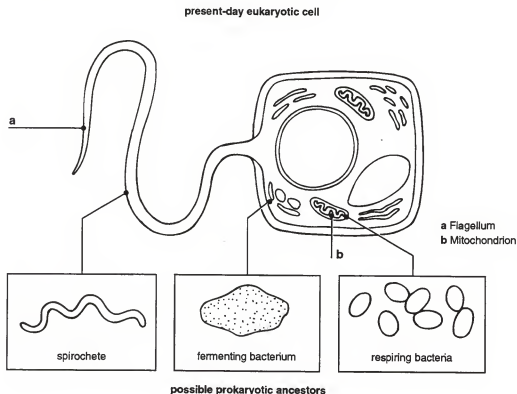
A whiplike extension of the cell membrane that propels the bacterium.

LYNN MARGULIS AND THE ENDOSYMBIOTIC THEORY

Lynn Margulis (born 1938) was professor of biology at Boston University from 1977 to 1988 and in the latter year became Distinguished Professor of the University of Massachusetts. Margulis studied the evolution of eukaryotes such as plants and animals. In her book *Origin of Eukaryotic Cells* (1970) Margulis put forward a theory described as "hereditary endosymbiosis."

This theory proposes that:

- Eukaryotes are essentially colonies of prokaryotes (bacteria).
- Various features of eukaryotic cells have evolved from free-living prokaryotes. These include the cellular organelles (miniorgans) mitochondria, chloroplasts, and flagella – all of which were once free-living bacteria. Flagella, for example, were once similar to spirochetes (spiral-shaped bacteria).
- The process of evolution from prokaryote to eukaryote began with a symbiotic (mutually dependant) relationship between an oxygen-using bacterium, the first mitochondrion, and a fermenting bacterium.
- These associated organisms might have been joined by a flagellumlike bacterium. This would have had the evolutionary advantage of providing locomotion.



These ingenious ideas remain hypothetical. As Margulis admits herself, proof could be obtained only if organelles from eukaryotic cells could be cultured outside of cells and then restored to a symbiotic relationship. This has not yet been achieved.

VIRUSES

Viruses are tiny, noncellular particles ranging from 0.01 to 0.3 μm in size. There is argument as to whether or not they should be regarded as living. This is because viruses are only capable of independent metabolism and reproduction when inside a host cell. For this reason, some scientists consider viruses to be living organisms while others do not.

STRUCTURE

Viruses differ greatly in shape and size but all share the same basic structure, which consists of a nucleic acid and a protein shell. Some viruses also have an outer envelope.

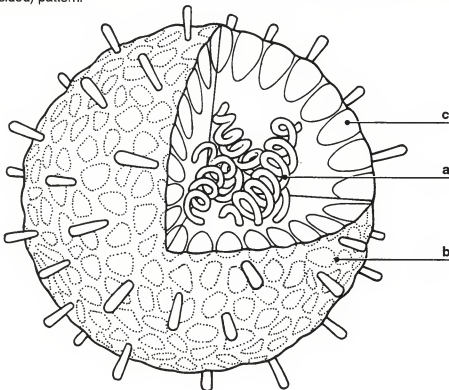
Nucleic acid

A core of nucleic acid (a) carries the viral genome – its complete set of genes. This is either DNA (deoxyribonucleic acid) or RNA (ribonucleic acid). The nucleic acid contains all the information necessary for viral replication. Viral genomes vary considerably. They may be:

- double-stranded or single-stranded;
- linear or circular; and
- of widely-varying size, from about 5,000- to 300,000-nucleotides (building blocks) long.

Capsid

A shell (capsid) (b) of protein molecules (c) surrounds the nucleic acid. The genome may be extended and surrounded by helically-arranged protein molecules to form a sphere; or it may be compacted and surrounded by a shell of protein molecules arranged precisely in an icosahedral (twenty-sided) pattern.

**FEATURES**

- Most viruses are too small to be seen with visible light (optical) microscopes.
- Viruses can synthesize viral proteins and undergo replication when inside the host cell by using the host's own facilities. This may cause the death of the cell. The clones produced by replication are released when the host cell's outer membrane is ruptured. Viruses can parasitize animal, plants, and bacterial cells in this way. As a result, they are highly destructive and can bring about many plant and animal diseases.

TYPES OF VIRUSES

Viruses are often named according to the hosts they attack. Adenoviruses, for example, attack the adenoid glands in humans. Bacteriophages attack bacteria. The table below organizes viruses into the main families that cause disease in humans.

VIRAL FAMILY	DISEASE OR CONDITION CAUSED BY VIRUS
a Adenoviruses	● eye infections ● respiratory infections
b Arenaviruses	● Lassa fever (a west African disease carried by rats)
c Coronaviruses	● common cold
d Herpesviruses	● genital herpes ● shingles ● cold sores ● glandular fever ● chickenpox
e Orthomyxoviruses	● influenza
f Papovaviruses	● warts
g Paramyxoviruses	● mumps ● measles ● rubella
h Picornaviruses	● respiratory infections ● hepatitis A and B ● myocarditis (heart-muscle inflammation)
i Poxviruses	● cowpox ● smallpox
j Retroviruses	● AIDS (acquired immune deficiency syndrome) ● possibly certain cancers ● degenerative brain diseases
k Rhabdoviruses	● rabies
l Togaviruses	● yellow fever ● encephalitis (inflammation of the brain)



RETROVIRUSES

Retroviruses are RNA (ribonucleic acid) viruses. They contain the enzyme (biological catalyst) reverse transcriptase. This allows them to make a complementary copy of their RNA and produce, in effect, strands of DNA (deoxyribonucleic acid). This allows them to carry out replication. Reverse transcriptase has attracted much attention. The discovery that DNA could be formed from RNA ran counter to the previously accepted dogma that the direction of transcription was always from DNA to RNA.

ONCOVIRUSES

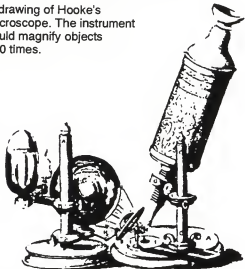
Host cells that have incorporated viral nucleic acid into their DNA might continue to reproduce. In some cases, they become cancerous. Viruses that have this effect are known as oncoviruses. The cancerous changes in cells are brought about by the introduction into the cell's DNA of viral genes known as oncogenes. Cancer may also be induced if viral genes activate dormant oncogenes normally present in the cellular genome. Oncoviruses belong to a variety of viral families.



ROBERT HOOKE DESCRIBES CELLS

The English scientist Robert Hooke (1635–1703) was curator of instruments at the Royal Society in London, of which he was a founder. In 1665, he published *Micrographia*. This book contained an account of observations he had made with a microscope designed by Hooke himself – one of the earliest optical (light) microscopes.

A drawing of Hooke's microscope. The instrument could magnify objects 270 times.



HOOKE'S DISCOVERY

In this book, he illustrated the microscopic structure of cork, showing woody walls surrounding empty spaces. These spaces were not, in fact, cells but merely the gaps left by cells. Hooke's importance, however, was that he effectively "discovered" cells and was the first to use the word "cell" in a biological context. It is said that he introduced the term



Hooke's drawing of cork cells that he published in *Micrographia* (1665).

because the walls of dead cork cells reminded him of the blocks of cells occupied by monks. Hooke also described similar structures in specimens from other trees and plants. He noted that in some samples the spaces ("cells") were filled with a liquid. He concluded – wrongly – that the function of the "cells" was to transport materials through the plant.

The significance of Hooke's discovery

During Hooke's lifetime and for well over a century afterward, no one appreciated the significance of the material inside the cell walls. Color fringing (chromatic aberration) produced by the simple lenses of the time precluded any adequate observations of the details of the cell contents. So it was nearly 200 years after the introduction of the microscope before any real advances were made in the understanding of the cell. These had to wait for the development of achromatic lenses using combined glasses of different refractive indexes. Such lenses were not introduced until about 1830.

SUBSEQUENT HISTORICAL HIGHLIGHTS

- The nucleus (control center) of the cell was observed, in 1833, by the Scottish plant taxonomist Robert Brown (1773–1858).
- This was then recognized as being a constant component of plant cells.
- Nuclei were then observed and recognized as such in some animal cells.
- In the later half of the 1800s, dyes were developed that stained the nucleus. It was found to be always involved in cell division.
- An apochromatic compound microscope was produced to the design of the German physicist Ernst Abbé (1840–1905) working in conjunction with the glass chemist Otto Schott (1851–1935).
- This microscope and others like it made major biological discoveries possible.
- An actively moving and streaming substance was observed within cells. This was called protoplasm. Its recognition made it clear that cells contain living material.

M. J. SCHLEIDEN, THEODOR SCHWANN, AND THE CELL THEORY

The German barrister, doctor of philosophy, doctor of medicine, and professor of botany Matthias Jacob Schleiden (1804–81) was the first to recognize the importance of cells. His work inspired the German biologist Theodor Schwann (1810–82) to take the matter further.

THE CELL THEORY

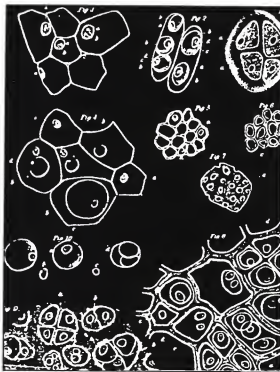
Through the work of these two men, the cell theory of biology was established. It states that cells are of universal occurrence and are the basic units of living organisms. This is one of the most central concepts in all biology.

- In 1838, Schleiden announced that all the various parts of plants were either made of cells or comprised the products of cells.
- He surmised that each cell of every tissue could be looked on as an independent unit, but it must also contribute to the life of the whole organism to which it belonged.
- In 1839, Schwann published a paper in which he extended Schleiden's idea to animals.

- Schwann also recognized that some organisms were unicellular, others multicellular.

Schleiden went on to research further.

- He recognized the importance of the cell nucleus (control center).
- He was mistaken, however, in believing that new cells budded off the surface of the nucleus.
- He also observed the active movement of the substances within the cell and called this "protoplasmic streaming." This made it clear that cells contain living material.



Schwann's drawings of plant and animal cells.

OTHER SIGNIFICANT DISCOVERIES

Schwann made many other important contributions to biology:

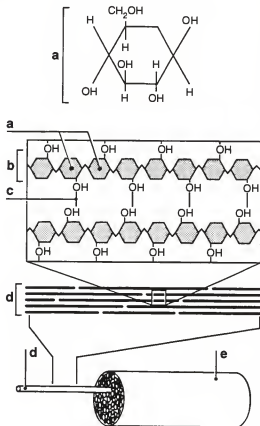
- He recognized that an ovum (egg) is a single cell that, after fertilization, divides repeatedly and develops into a complex organism.
- He isolated a digestive enzyme (biological catalyst) from the stomach lining and named it pepsin. He recognized that pepsin was responsible for protein digestion.
- He proved that fermentation of sugar was the result of living yeast cells.
- He provided strong evidence to counter the theory of spontaneous generation of life in putrefying organic material.
- He coined the term "metabolism" for the chemical changes occurring in living tissues.
- He discovered the cells that make up the myelin sheath of nerve cell axons. These are known to this day as Schwann cells.

PLANT CELL WALL 1: STRUCTURE

Plant cell walls are nonliving structures secreted by living cells while they are still enlarging. They consist mainly of cellulose. The plant cell wall should not be confused with the cell (plasma) membrane, which is common to most cells.

CELLULOSE

- Cellulose is a polysaccharide (a molecule made up of many chains of sugar units). Its building blocks are units (monomers) of a type of glucose (a sugar) called β glucose (a).
- Between 300 and 15,000 of these monomers (a) are joined head-to-tail in a chain (b). This arrangement ensures that the OH (hydroxyl) groups project from each side of the chain.
- These OH groups can then form hydrogen bonds (c) with neighboring chains. Several chains linked together by these cross-linkages form a cellulose molecule (d).

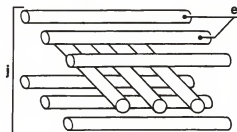
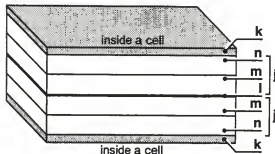
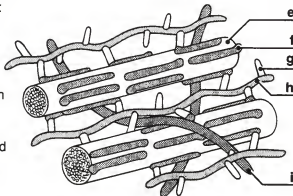


MICROFIBRILS

- Several cellulose molecules (d) are arranged in a structure called a microfibril (e). Each microfibril comprises about 60 to 70 cellulose chains and is roughly 3.5 nm wide.
- Microfibrils (e) are embedded in a gel-like fluid that contains the polysaccharides hemicellulose (f) and pectins (g and h), and some glycoproteins (proteins combined with carbohydrate sugars) (i).

THE PLANT CELL WALL

- In a plant cell wall (j), microfibrils (e) are often arranged in successive layers that lie at right angles to each other.
- The cell wall (j) appears between the cell membrane (k) and the middle lamella (l) — the mainly pectin "cement" that holds cells together. The cell wall may be divided into an outer primary cell wall (m) and an inner secondary cell wall (n).
- In some cells, the secondary wall is hardened with lignin (a cellulose-like substance). This creates wood.



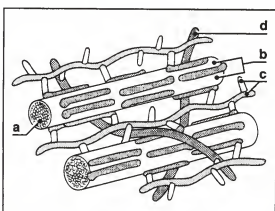
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PLANT CELL WALL 2: FUNCTIONS**CELL SHAPE**

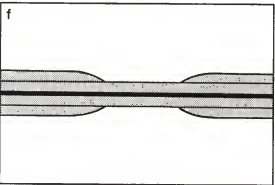
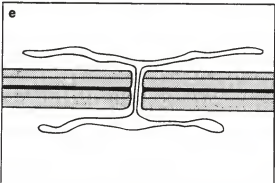
- The main function of the cell wall is to provide rigidity and shape to the cell. This, in turn, gives the plant its shape and makes the stem stiff.

CELL STRENGTH AND PROTECTION

- Cross-linkages within the cellulose molecules themselves (a) and between the microfibrils (b), pectins (c), and hemicelluloses (d) give the cell wall its great strength. This protects the cell and provides its external barrier.

**TRANSPORT OF SUBSTANCES**

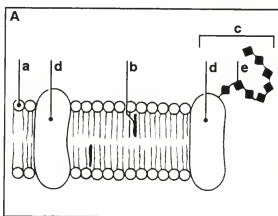
- In spite of the thickness and density of the cell wall, it has minute water-filled channels that allow the diffusion of water and nutrients in and out of the cell. These channels are a type of cell junction called plasmodesmata (e).
- The cell wall also has thinned areas called pits (f) through which threads of cytoplasm (semifluid mixture) penetrate from cell to cell. These allow the freer passage of molecules between cells.
- Secondary cell walls only occur in cells that are relatively fixed in structure and are not growing or engaged in a great deal of activity. They are, therefore, a feature of supportive and water-conducting plant tissue.
- Where lignin occurs it increases the toughness of the wall and makes it waterproof. The result is that the cell cannot receive nutrients and therefore dies. These cells become fluid-filled spaces that function in water-conducting tissues.



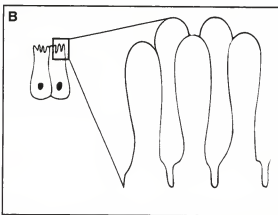
CELL MEMBRANE 1: STRUCTURE, PROJECTIONS, AND JUNCTIONS**STRUCTURE****A Lipid bilayer**

Basically, the cell (plasma) membrane is formed by a lipid bilayer. This fatty double layer contains:

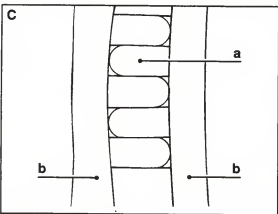
- a phospholipids (fat molecules containing phosphorus);
- b cholesterol (a type of steroid); and
- c glycoproteins, which are made up of d protein and e carbohydrate (sugar) on the extracellular (outer) surface of the protein.

**MEMBRANE PROJECTIONS****B Microvilli**

These are tiny, fingerlike projections, or folds, of the cell membrane itself.

**MEMBRANE JUNCTIONS****C Tight, or impermeable, junction**

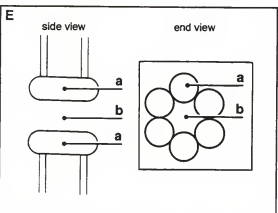
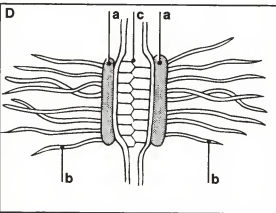
This is formed by protein molecules (a) of neighboring cell membranes (b) fusing together.

**D Anchoring junction**

At these junctions, on the insides of the neighboring cells, are rivetlike thickenings called plaques (a). These are attached to the opposite side of the cell membrane by keratin filaments (strong, flexible protein strands) (b). Linker proteins (c) extend from the plaques and cross the space between the cells.

E Communicating junction

Transmembrane proteins (a) are arranged into groups (connexons) with hollow channels (b) at the center.



CELL MEMBRANE 2: FINE STRUCTURE

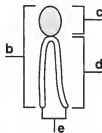
The cell (plasma) membrane is made up of a variety of molecules, including phospholipids, proteins, and cholesterol. Most of these are able to move about within the membrane.

PHOSPHOLIPIDS

A double layer (a), about 5 nm thick, of phospholipid molecules comprises much of the cell membrane.

Structure

Phospholipids (b) are modified lipids (fats) that contain phosphorus. They are divided into two main parts; a head (c) and a tail (d).



● **The head** is the phosphorus containing part of the molecule. As this part of the molecule bears an electrical charge, it is polar and therefore attracts other polar (charged) particles, such as water and ions.

● **The tail** consists of two chains (e) of fatty acids. They are nonpolar and therefore only interact with other nonpolar particles.

As the polar heads are water-seeking (hydrophilic) and the nonpolar tails are water-repelling (hydrophobic), the phospholipid molecules orient themselves with their heads pointing outward and their tails in contact.

PROTEINS

f Intrinsic proteins pass through the membrane and protrude on either side.

g Extrinsic proteins are attached to the surface or one half of the lipid bilayer.

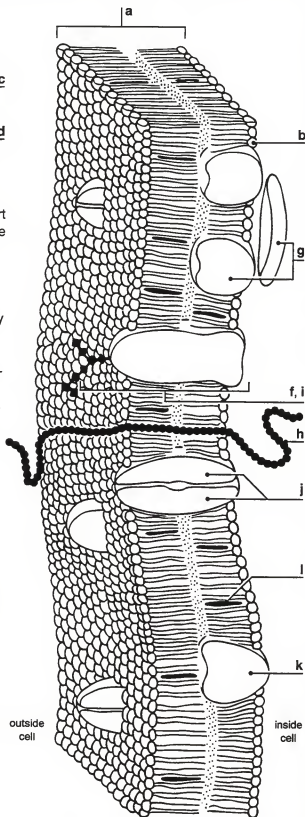
h Structural (or fibrous) proteins are strandlike and connect to the cell's cytoskeleton. They may also connect the cell to adjacent cells or to the extracellular matrix (material outside the cell).

Functional (or globular) proteins are generally spherical and include:

- sensors and receptors – glycoproteins, for example (i);
- enzymes (biological catalysts); and
- transport proteins – channel proteins (j) and carrier proteins (k).

CHOLESTEROL

Cholesterol (l) is a sterol, which is a type of steroid.



CELL MEMBRANE 3: OVERVIEW OF FUNCTIONS

FUNCTIONS	STRUCTURES	1	1 Lipid bilayer a Phospholipid molecule b Cholesterol molecule c Structural protein d Cytoskeleton e Transport protein f Protein receptor g Hormone h Glycoprotein
Framework/support of cell	<ul style="list-style-type: none"> Cholesterol (1b) provides stability. Structural proteins (1c) such as keratin and collagen give strength and may be attached to the cytoskeleton (1d). Membrane junctions (2) knit neighboring cells together. Anchoring junctions (2b) distribute tension throughout tissues, helping to prevent tearing. 		
Barrier	<ul style="list-style-type: none"> Phospholipid and cholesterol molecules (1a, b) are relatively impermeable to water-soluble molecules. Tight junctions (2a) prevent molecules from passing between cells. 		2 Membrane junctions a Tight junction b Anchoring junction c Gap junction
Transport	<ul style="list-style-type: none"> Transport proteins (1e) enable substances to pass in or out of the cell by various means. Gap junctions (2c) allow the passage of substances from one cell to another. 		
Increasing absorptive capacity of cell	<ul style="list-style-type: none"> Microvilli (3) increase the surface area and absorptive capacity of the cell. 		3 Microvilli
Receptor sites/Intercellular communication	<ul style="list-style-type: none"> Proteins (1f) are binding sites for hormones (regulatory chemicals) (1g). Glycoproteins (1h) act as receptors for bacteria, viruses, and toxins (poisons); determine blood type; and play a role in cell-to-cell interactions. 		

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OVERVIEW OF PASSIVE TRANSPORT

In passive transport, the cell does not use energy to transport substances across its membrane.

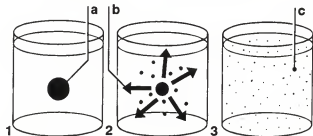
MECHANISM**EXAMPLES OF SUBSTANCES TRANSPORTED****Simple diffusion**

1-2 Particles in solution diffuse from an area of higher concentration (a) to one of lower concentration (b).

3 They do so until they are evenly distributed (c).

Particles will diffuse across a cell membrane if they are small enough to pass through membrane pores or if they are lipid (fat) soluble.

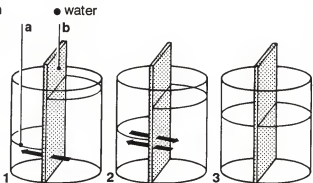
- fats
- carbon dioxide
- oxygen
- chloride

**Osmosis**

Simple diffusion of water molecules through a semipermeable membrane from a region of higher solute concentration.

1-2 Water molecules (a) diffuse through the pores of a semipermeable membrane (b) until

3 they are evenly distributed on both sides of the membrane.

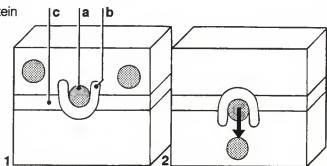
**Facilitated diffusion**

Diffusion of larger, lipid-insoluble particles using a carrier protein.

1 The particle (a) binds to the carrier protein (b) straddling the cell membrane (c).

2 The particle enters the cell through the protein.

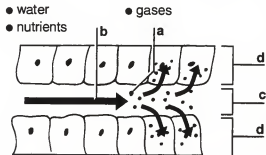
- glucose (a sugar)
- fructose (fruit sugar)



Alternatively, particles may diffuse through a water-filled channel formed by channel proteins.

Filtration

Particles (a) are forced through the cell membrane by hydrostatic (fluid) pressure (b) from an area of higher pressure (c) to one of lower pressure (d).



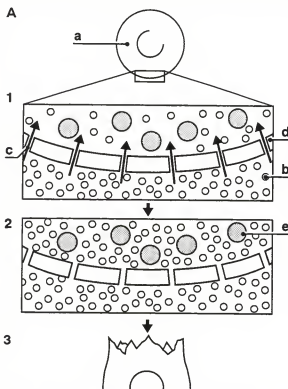
OSMOSIS AND OSMOREGULATION 1

With a sufficient concentration gradient (difference between the concentration of solutes either side of the membrane), almost any molecule will, in time, diffuse across a cell (plasma) membrane by simple osmosis. The rate of diffusion depends on the gradient, the size of the molecule, and its lipid (fat) solubility. Nonpolar – and therefore hydrophobic (water-repelling) – molecules can pass quickly. The hydrophobic tails of the phospholipid molecules that make up the cell membrane greatly retard the passage of most polar molecules, however (water and ions, for example). This is essential if cells are to maintain internal concentrations of dissolved substances that are different from those in the external environment.

EFFECTS OF OSMOSIS ON ANIMAL CELLS

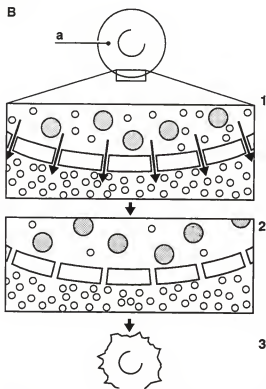
A Hemolysis

- 1 If a red blood cell (a) is placed in pure water, water molecules (b) diffuse through pores (c) in the cell (plasma) membrane (d) by osmosis.
- 2 The red blood cell takes in water until there is an equal concentration of water molecules on the inside of the cell as on the outside of the cell. This lowers the concentration of essential solutes (e) inside the cell and causes the cell to swell.
- 3 The red blood cell bursts. This is known as hemolysis.



B Crenation

If the cell (a) is placed in a strong salt solution, however, it shrinks and becomes crinkled as it loses water molecules to the surrounding environment (steps 1–3). This is known as crenation.



EXAMPLES OF OSMOREGULATION IN ANIMALS

The process by which an organism maintains the correct balance between water and solutes is known as osmoregulation.

- In animal cells, the sodium-potassium pump (see 3.12) helps to regulate osmosis. There is a constant tendency for sodium (a salt) to leak into the cell. This alters the osmotic balance. By driving out sodium, the pump helps to prevent crenation or hemolysis.
- In mammals, osmoregulation is carried out by the urinary system.

OSMOSIS AND OSMOREGULATION 2

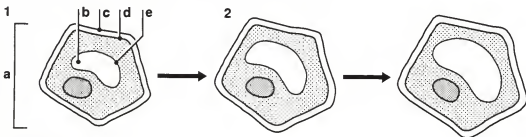
EFFECTS OF OSMOSIS ON PLANT CELLS

Turgidity

1 If a partially-turgid (swollen) plant cell (a) is placed in pure water, its vacuole (b) fills with water, as water molecules are able to flow through the cell wall (c), cell (plasma) membrane (d), and tonoplast (vacuole membrane) (e) by osmosis.

2 The cell swells. It does not burst, however, as the cell wall is able to stretch to a certain degree. When the cell wall is stretched to its limit, internal hydrostatic (fluid) pressure prevents the uptake of any more water – the cell is fully turgid.

Turgor is important in plants. It allows them to maintain their shape and form. Some plants – insectivorous ones, for example – have cells that are able to rapidly adjust their turgidity, allowing movement of leaves to catch insects.

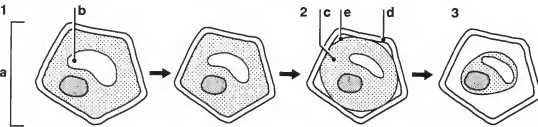


Plasmolysis

1 If a plant cell (a) is placed in a strong sucrose (sugar) solution, water flows out of its vacuole (b) by osmosis and the volume of the cell decreases.

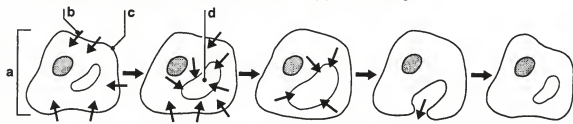
2 The cytoplasm (semifluid mixture) (c) starts to pull away from the cell wall (d), leaving a gap between the cell wall and cell membrane (e).

3 When the cytoplasm has completely withdrawn from the cell wall, plasmolysis has been reached.



EXAMPLES OF OSMOREGULATION IN PLANTS AND PROTISTS

- Depending on their natural environment, plants have a variety of mechanisms to preserve water or to rid themselves of excess water. These include the shape and form of leaves and roots, the production of seeds and spores, the secretion of excess water or salt, and the shedding of leaves.
- Unicellular protists have a contractile vacuole that carries out osmoregulation. For example, an amoeba (a) may take up water molecules (b) by osmosis through its cell membrane (c). Excess water is collected by a contractile vacuole (d) and discharged.



OVERVIEW OF ACTIVE TRANSPORT

In active transport, the cell uses energy in the form of the cellular-energy storage molecule, ATP (adenosine triphosphate) to transport substances across its wall if a particle:

- is too large to pass through the membrane pores;

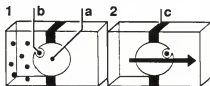
- cannot dissolve through the lipid bilayer (fatty double layer) of the cell membrane; or
- needs to be moved "uphill" (from an area of lower concentration or pressure to an area of higher concentration or pressure).

MECHANISM**Solute pumping**

- 1 A carrier protein, called a solute pump (a), powered by ATP, combines with the particle (b).
- 2 It transports it across the cell membrane (c).

EXAMPLES OF SUBSTANCES TRANSPORTED

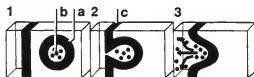
- amino acids (building blocks of proteins)
- most ions

**Exocytosis**

Secretion of substances from a cell.

- 1 A membrane-covered vesicle (a) carries the substance (b).
- 2 It fuses with the cell membrane (c).
- 3 The particle is ejected.

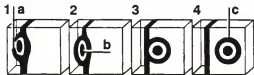
- hormones (regulatory chemicals)
- mucus (thick, slimy fluid)
- waste materials

**Endocytosis: phagocytosis**

"Eating" or engulfing of particles by a cell.

- 1 Part of the cell membrane (a) protrudes.
- 2 It engulfs a particle (b).
- 3-4 The sac (c) formed separates from the cell membrane. Enzyme-containing sacs (lysosomes) then digest the contents.

- foreign bodies such as bacteria and viruses

**Endocytosis: pinocytosis**

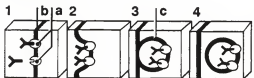
Similar to phagocytosis, but it is used to transport fluids across the cell membrane.

- water and various solutes
- liquids containing proteins and fats

**Receptor-mediated endocytosis**

- 1 Proteins (a) in the cell membrane act as receptor sites for certain particles.
- 2-4 Once a particle is attached, the membrane folds inward and the small sac created (c) separates from the main cell membrane.

- hormones
- iron
- cholesterol (a steroid)



JENS SKOU AND THE SODIUM-POTASSIUM PUMP

A feature of great importance in animal cells is the movement in and out of them of sodium and potassium ions, which is carried out by the sodium-potassium pump. Since the 1950s, Jens Skou (born 1918) has been studying the sodium-potassium pump. His work has contributed greatly to the understanding of this active (energy-using) transport mechanism.

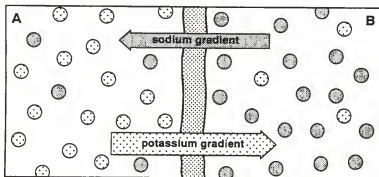
SODIUM AND POTASSIUM GRADIENTS

A Inside most cells, the concentration of potassium ions (K^+) is 10 to 20 times higher than outside the cell.

B Outside most cells, the concentration of sodium ions (Na^+) is 10 to 20 times higher than inside the cell.

Key:

-  Sodium ion
-  Potassium ions
-  Cell membrane



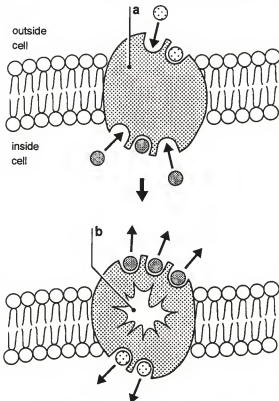
These ions are continuously, though slowly, leaking through the cell (plasma) membrane along their gradients – sodium at a slower rate than potassium, as the cell membrane is slightly less permeable to sodium than potassium. A mechanism is therefore needed to maintain the above levels on either side of the membrane:

- if excitable cells such as muscle and nerve cells are to function normally, and
- if body cells are to maintain their normal fluid volume – by regulating osmosis.

This is achieved by the sodium-potassium pump.

THE SODIUM-POTASSIUM PUMP

- An enzyme (biological catalyst) called Na^+-K^+ ATPase (**a**) acts as the pump.
- It is powered by ATP (adenosine triphosphate) (**b**) – the cellular-energy storage molecule.
- In one go, this pump can transport three sodium ions out of the cell and two potassium ions back into the cell; this ensures that there are more potassium ions inside the cell than outside and that the reverse is true for sodium.
- All these ions are moved against their concentration gradients.
- The pump has to function almost continuously to maintain the correct levels of these ions either side of the cell membrane.
- The energy required to fuel the pump is considerable. Nearly a third of the energy expenditure of a typical cell occurs in keeping this pump operating. In the case of electrically-active cells such as nerve cells, it uses up to two-thirds of the total energy.

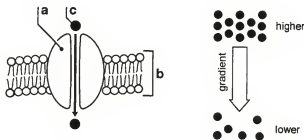


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ACTIVE AND PASSIVE TRANSPORT PROTEINS

CHANNEL PROTEINS

Groups of channel proteins (a) are believed to form a water-filled conduit through the cell (plasma) membrane (b). Specific molecules (c) can then diffuse down this channel. This is facilitated diffusion.



- Transport by channel proteins is always passive, as they do not use the cell's own energy.
- The diffusion is always along concentration gradients – from a region of higher concentration to a region of lower concentration.
- The only energy employed is kinetic (energy of motion), which is generated by the constant movement of the molecules to be transported.

CARRIER PROTEINS

Passive carriers

Many carrier proteins allow the passive movement of uncharged molecules from a higher to a lower region of concentration.

Active carriers

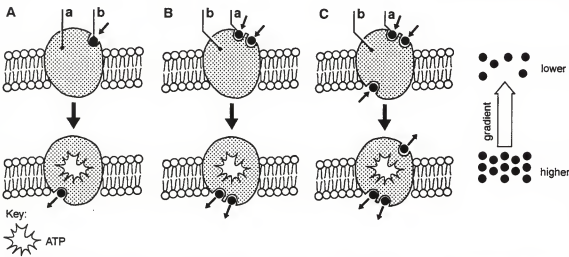
In order to move molecules against a concentration or an electrical gradient, active transport is required. This is always done by carrier proteins using the cell's own energy – ATP (adenosine triphosphate), the cellular-energy storage molecule. The mechanism of active transport by carrier proteins is complex and not yet fully understood. It is believed to involve specific binding sites at which certain reactions occur that lead to a change in the formation of the protein, allowing the movement of the molecule into the cell.

A Uniports An active carrier protein (a) that transports only one molecule (b) at a time is a uniport.

Coupled transporters move more than one substance at the same time.

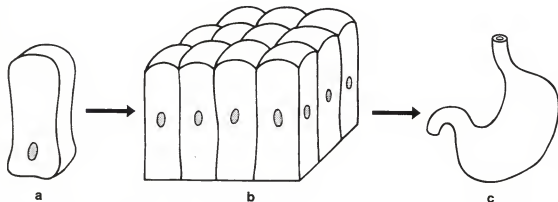
B Symports If the two transported substances (a) are moved in the same direction, the protein (b) is a symport.

C Antiports If the substances (a) travel in opposite directions, the protein (b) is an antiport – the sodium-potassium pump is an antiport, for example (see 3.12).



INTERCELLULAR SUPPORT

In multicellular organisms, most of the cells (a) are organized into tissues (b). These are collections of similar cells held together into a relatively fixed structure and capable of carrying out one or more particular functions. Different tissues, in turn, are collected and joined together to form organs (c). The extracellular matrix (material outside cells), connective tissues, and intercellular junctions hold these tissues together.

**EXTRACELLULAR MATRIX**

Cells grouped together as tissues are normally held together in a scaffolding known as the extracellular matrix – a nonliving material made up of fibers and ground substance.

Fibers

Fibers are embedded in the ground substance. There are three main types: collagen, elastic, and reticular.

Collagen fibers are made of the strong, flexible protein collagen. They give strength and resistance to the tissue.

Elastic fibers are made up of the stretchy protein elastin. They allow the tissue to stretch and recoil.

Reticular fibers are very thin, many-branched fibers made of reticulin (thin collagen fibers). They form fine, supporting networks.

Ground substance

This is water with nonfibrous proteins and other molecules in it. These act as a glue that holds the tissue together.

CONNECTIVE TISSUE

The extracellular matrix may often be more profuse than the cells embedded in it. In such cases, the tissue is often described as

connective tissue. Variations in the nature of the extracellular matrix and the types of cell found determine the type of connective tissue.

INTERCELLULAR JUNCTIONS

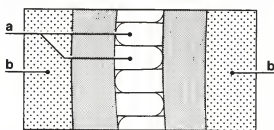
In addition to the extracellular matrix, there are commonly direct cell-to-cell adhesions called junctions, which help to hold tissues together. There are three main types of intercellular junctions:

- tight junctions;
- anchoring junctions; and
- communicating junctions, including gap junctions, plasmodesmata, and synapses.

INTERCELLULAR JUNCTIONS 1: TIGHT JUNCTIONS

STRUCTURE

Tight, or impermeable, junctions are formed by protein molecules (a) of neighboring cells (b) fusing together like a zipper. There is no intercellular space between cells at a tight junction.

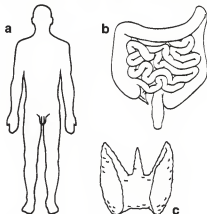


LOCATIONS

Tight junctions are found in epithelial tissues, which only occur in animals. These tissues:

- cover the body surface as skin (a);
- line internal cavities (b); and
- form glands (c).
- A special type of epithelial tissue called endothelium lines the walls of the heart, blood, and lymph vessels. In the brain, the endothelial cells of capillaries (the smallest blood vessels) have tight junctions.

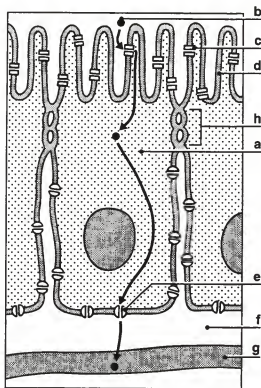
Tight junctions between epithelial cells are formed only between those parts of the cell junctions near the free surface.



FUNCTIONS

Transport proteins and tight junctions

- Epithelial cells transport substances required by the organism across their cell (plasma) membranes. An epithelial cell (a) in the intestine, for example, absorbs digested nutrients (b) through its external surface.
- This is carried out by transport proteins (c) located in the cell membrane (d).
- Nutrients then diffuse out of the cell through a different type of carrier protein (e) and into the extracellular matrix (f) on the inside of the epithelial tissue, and then into a blood vessel (g).
- The proteins that allow passage of molecules into the cells must be kept separate from those that allow passage out of the cell. The presence of tight junctions (h) near the free surface is thought to maintain this separation. Without the tight junctions, the "entry" proteins could migrate into the region of the "exit" proteins.



Blood-brain barrier

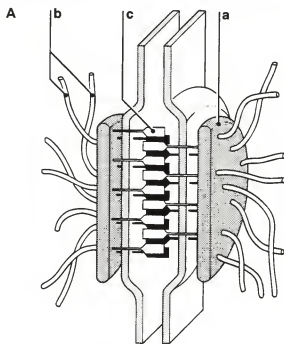
- Brain cells need to be protected from chemical variations in the surrounding environment. Otherwise the neurons would fire uncontrollably.
- The blood-brain barrier provides this protection.
- The main component of this barrier is provided by the capillary endothelium.

- Endothelial cells are almost totally joined together by tight junctions, making the capillaries relatively impermeable to unwanted substances.

INTERCELLULAR JUNCTIONS 2: ANCHORING JUNCTIONS

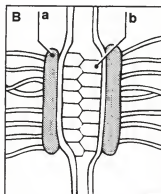
A STRUCTURE

At an anchoring junction, on the insides of the neighboring cells, are rivetlike thickenings called plaques (a). Each plaque is formed by an intracellular attachment protein. Attaching them to the opposite sides of the cell (plasma) membranes are keratin filaments (strong, flexible protein strands) (b). These filaments are part of the cell's cytoskeleton. Thin proteins (c) extend from the plaques and cross the space between the cells. These are called transmembrane linker proteins.



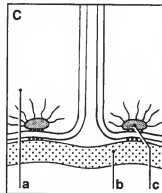
B Desmosomes

In cases where the plaques (a) are linked by intermediate (b) rather than thin filaments, the junction is known as a desmosome. In desmosomes, the linker proteins are called cadherins.



C Hemidesmosomes

Many sheets of epithelial (lining and covering) cells (a) lie on a noncellular basement membrane known as the basal lamina (b). Anchoring junctions (c) that link the epithelial cells to the basal lamina are called hemidesmosomes.



LOCATIONS

Anchoring junctions only occur in animals. Plants have a strong extracellular matrix (material surrounding cells) reinforced with cellulose and other substances, so they do not need anchoring junctions.

Tight junctions occur in epithelial (lining and covering) and muscular tissues, and they are particularly abundant in:

- skin epithelia;
- the cervix (the neck of the uterus); and
- cardiac (heart) muscle.

Intercalated discs

Together with gap junctions (see 3.17), desmosomes form intercalated discs (complex junctions) between cardiac muscle cells.

FUNCTIONS

- Anchoring junctions bind cells together in sheets or masses that form strong structural units.
- The networks that these junctions form in tissues distribute tension, helping to prevent tearing. This is why anchoring junctions are

prevalent in areas that are subjected to the mechanical stress of pulling and stretching.

- Within intercalated discs, for example, desmosomes prevent adjacent cells from separating during heart contractions.

INTERCELLULAR JUNCTIONS 3: COMMUNICATING JUNCTIONS

There are three main types of communicating junctions:

- gap junctions;
- synapses (nerve cell junctions) (see 3.40); and
- plasmodesmata.

GAP JUNCTIONS**Structure**

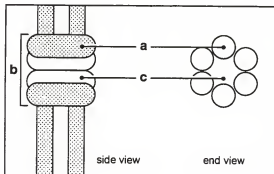
Transmembrane proteins (a) are arranged into groups (connexons) (b) with hollow channels (c) at the center. A gap junction comprises several hundred connexons.

Locations

Gap junctions occur in large numbers in most animal tissues.

Functions

- Gap junctions form channels through which water, ions, and small molecules can pass from one cell to the next. This allows both the chemical and electrical coupling of cells.



- In embryonic (unborn, developing) organisms, gap junctions enable nutrients to be distributed before the circulatory system is developed.

PLASMODESMATA**Structure**

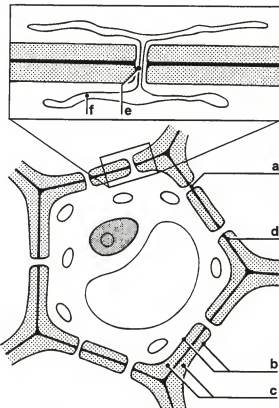
Plasmodesmata (a) are gaps of 20–40 nm diameter that pass clear through the cell membranes (b) and cell walls (c) of adjacent cells, as well as the middle lamella (d) between the cells. Through the center of each plasmodesma passes a fine cylindrical structure called a desmotubule (e). This is continuous, at each end of the channel, with the endoplasmic reticulum (f) of the neighboring cells.

Location

Plasmodesmata link all plant cells.

Functions

- The cell membranes of adjacent cells are continuous with each other as a lining of the plasmodesma channel. In this way, all the cells of a plant are in fluid communication with each other.
- Like gap junctions, the plasmodesmata form channels that allow water, ions, and small molecules to pass from one cell to the next, allowing both the chemical and electrical coupling of cells.
- Plasmodesmata give continuity to the



cytoplasm of adjacent cells, so water is able to diffuse from cell to cell.

- Plasmodesmata also give continuity to the endoplasmic reticulum of the entire plant.

CYTOPLASM

The cytoplasm (semifluid mixture) (a) is the cellular material outside the nucleus (control center) (b) and inside the cell (plasma) membrane (c). In eukaryotes, such as plants and animals, it consists of cytosol (gel-like fluid), cytoplasmic organelles (miniorgans), and inclusions (chemical substances). Prokaryotes (bacteria) have a cytoplasm and inclusions, but no organelles. As a whole, the cytoplasm:

- assists in the movements of organelles and transport of substances within the cell;
- provides an environment in which chemical reactions can occur; and
- helps to support and shape the cell.



CYTOSOL

Structure

This is a gel-like, semitransparent fluid comprising largely water. It contains dissolved proteins, sugars, salts, and other solutes.

of both a solute and a colloid.

As a solute, the cytosol stores many vital substances until they are needed.

As a colloid, the cytosol is able to change from a semifluid to a more solid state. This is important for many cell functions, including cell division.

Functions

The cytosol holds the other elements of the cytoplasm in suspension. It has the properties

CYTOPLASMIC ORGANELLES

There is a great variety of organelles. They include:



centrioles
(see 3.19)



endoplasmic
reticulum (ER)
(see 3.26)



nuclei
(see 3.32–33)



chloroplasts
(see 3.20)



Golgi apparatus
(see 3.27–28)



peroxisomes
(see 3.34)



cilia and flagella
(see 3.21–22)



lysosomes
(see 3.29)



ribosomes
(see 3.35)



the cytoskeleton
(see 3.23–24)



mitochondria
(see 3.30)



vacuoles
(see 2.07)

Structure

Except for the cytoskeleton and ribosomes, most organelles are enclosed in a membrane. Which ones are present in a cell and how many depends on the type of cell and the organism it appears in.

Functions

These tiny organs are the machinery of the cell. Each one has a particular function. The fact that most are membrane enclosed ensures that they can maintain an internal environment that is different from the rest of the cell. This allows them to carry out their particular tasks.

INCLUSIONS

These are chemical substances such as stored nutrients. The type of inclusion depends on the cell type. In adipocytes (fatty cells), for

example, the lipid (fat) droplet is an inclusion. Pigments (colorings) such as melanin in skin cells also count as inclusions.

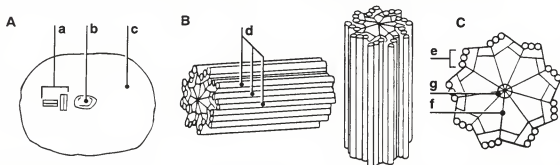
CENTRIOLES

STRUCTURE

A Centrioles (a) are a type of organelle (miniorgan) found inside animal cells and some simple plants. They occur in pairs and lie at right angles to each other near the nucleus (control center) (b) of the cell (c).

B Each centriole is a bundle of microtubules (tiny tubes) (d).

C The microtubules are arranged in nine groups of three (e) around protein spokes (f) radiating from a central axis (g).



FUNCTIONS

Cilia and flagella formation

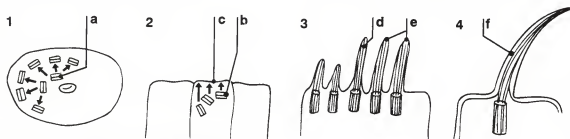
Centrioles form the bases of cilia and flagella (projections from the cell).

1 The centrioles (a) multiply.

2 The newly produced basal bodies (b) migrate to the cell membrane (c).

3 Each basal body sprouts microtubules (d) that push the cell membrane outward to form cilia (e).

4 A flagellum (f) results when microtubules form a longer, usually singular, projection.



Spindle formation during cell division

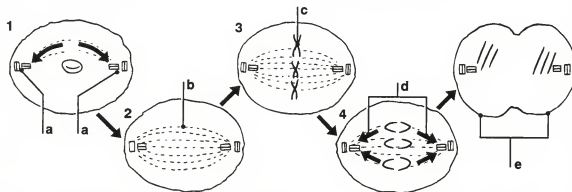
Centrioles form a spindle (a delicate network) during cell division.

1 Centrioles reproduce, and each pair (a) migrates to opposite ends of the cell.

2 Fibers extend between the pairs of centrioles to form a spindle (b).

3 Replicated chromosomes (c) line up in the middle of the spindle.

4 The fibers of the spindle retract (d) toward the centrioles, splitting the X-shaped chromosomes, which are packaged into two new daughter cells (e).

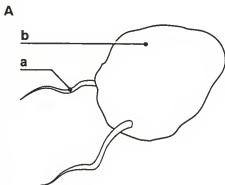


CILIA AND FLAGELLA 1: LOCATION AND STRUCTURE

LOCATION

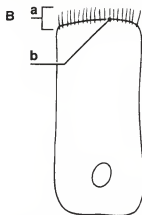
A Flagella

Flagella (a) are found on the surface of certain cells (b), such as sperm and some protists (unicellular organisms). They can occur singly – as on human sperm – or in small groups on the cell. Bacterial flagella are structurally different and do not fall within this category.



B Cilia

Cilia (a) are found on many animal cells and also occur on a few plant cells. They are a common feature of epithelium (lining and covering tissues). Cilia appear as tiny, hairlike fronds on the cell's exposed surface (b). They do not occur singly.

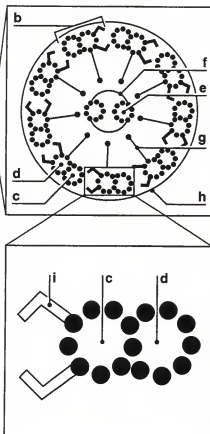


STRUCTURE

- Both flagella and cilia have the same fine, whiplike structure, but flagella are often longer.
- Each cilium or flagellum (a) is made of nine pairs (b) of microtubules (tiny tubes).
- One of each pair is complete (c), while the other (d) is incomplete but fused to its companion.
- These pairs of microtubules are arranged in a circle, forming a tubular structure.
- The nine doublet pairs surround a single, central pair (e) of unattached microtubules. This axial pair is enclosed in a sheath (f).
- Nine protein spokes (g) radiate from the sheath to the nine outer doublets. The whole structure is covered by the cell (plasma) membrane (h).
- Some of the microtubule proteins are purely structural and hold adjacent bundles together; others are contractile and provide movement. The main moving protein is called dynein. This appears as arms (i) attached to a microtubule.



cross-section through a cilium or flagellum



CILIA AND FLAGELLA 2: FUNCTIONS AND MOTION

FUNCTIONS

Cilia

Cilia's wavelike movement enables them to carry matter or fluid in one direction over a cell's surface.

- In the airways of humans, for example, cilia move mucus (thick, slimy fluid) toward the throat to be removed by swallowing. This gets rid of dust and bacteria trapped in the mucus and helps clean and protect the lining

of the respiratory tract.

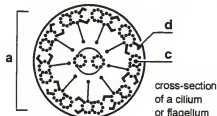
- Ciliated cells can also move fluids, so that nutrients can be carried into the organism.
- Cilia are common on protists as a source of motility.

Flagella

Flagella are used to move the cell itself.

MOTION

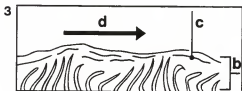
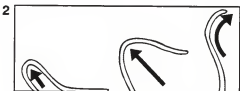
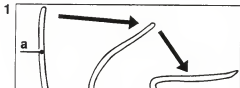
Movement of a cilium or flagellum (a) is generated by the internal dynein "arms" (b). These arms grip adjacent microtubules (c) and crawl along their length. This causes the paired microtubules to bend, forcing the cilium or flagellum to bend in turn.



Ciliary motion

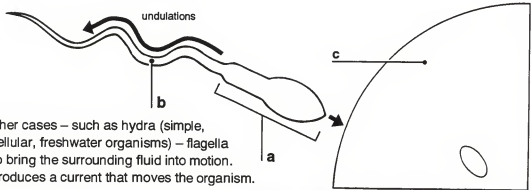
As a cilium moves, it alternates between a power stroke and a recovery stroke.

- 1 Power stroke** The nearly straight cilium (a) moves in an arc. This stroke is propulsive.
- 2 Recovery stroke** The cilium bends and returns to its original position. This stroke is nonpropulsive.
- 3 Propulsion** With these two strokes, many cilia moving together (b) propel a substance (for example, mucus) (c) in one direction (d) across the cell's surface.



Flagella motion

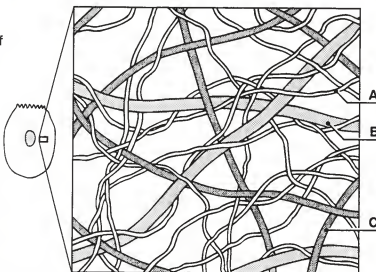
Flagella usually provide motility by a lashing action. Undulations pass along the flagellum from base to tip, driving the organism in the opposite direction. For instance, a human sperm (male sex cell) (a) uses its flagellum (b) to propel itself toward the female egg cell (ovum) (c). (Sperm are the only human cells that have flagella.)



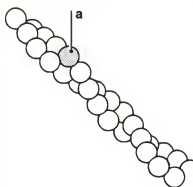
In other cases – such as hydra (simple, multicellular, freshwater organisms) – flagella beat to bring the surrounding fluid into motion. This produces a current that moves the organism.

CYTOSKELETON 1: STRUCTURE

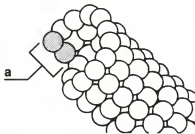
The cytoskeleton is a kind of intracellular scaffolding. It consists of a complex network of tiny protein fibers and tubes suspended in the cytosol (gel-like fluid) inside a cell. The cytoskeleton is a dynamic structure that is constantly changing as the cell grows and especially when it divides. It comprises three types of protein structures: microtubules (tiny tubes); microfilaments (tiny fibers); and intermediate filaments. None of these have a covering membrane.

**A MICROFILAMENTS**

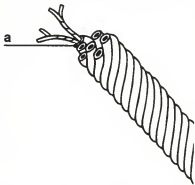
- Microfilaments are thin strands of the protein actin.
- They are 5–9 nm wide.
- The actin subunits (a) are arranged in two chains that twist around each other, forming a helical (coiled) molecule.
- Actin has the ability to contract (or shorten).
- Microfilaments form bundles, flat meshes, or three-dimensional networks attached to the inside of the cell (plasma) membrane.
- They are found most abundantly at the periphery of the cell, just under the cell membrane.
- Microfilaments are frequently being broken down and reassembled.

**B MICROTUBULES**

- Microtubules are hollow cylinders of the protein tubulin.
- They are about 20–25 nm wide.
- The tubulin subunits (a) are spherical.
- Microtubules radiate from the centromere (cell center).
- They are frequently being broken down and reassembled.
- Organelles (miniorgans) are arranged along the microtubules.

**C INTERMEDIATE FILAMENTS**

- These are ropelike fibers made from a considerable range of proteins called intermediate filament proteins (a).
- They are about 10 nm wide.
- These filaments extend throughout the cytoplasm. They are attached to the cell membrane and may span the cell from one side to the other.
- Intermediate filaments also form a meshwork inside the nucleus (control center).
- Intermediate filaments are the most permanent and stable part of the cytoskeleton.



CYTOSKELETON 2: FUNCTIONS

The cytoskeleton acts as the "bones" and "muscles" of the cell by:

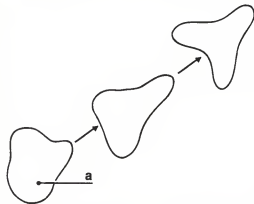
- supporting the cell's shape and organelles, and
- helping to generate movement within the cell and of the cell itself.

The component parts of the cytoskeleton each have particular roles to play.

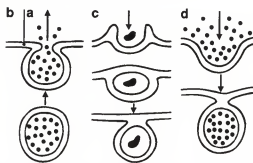
STRUCTURE	FUNCTIONS
Microtubules	<ul style="list-style-type: none"> ● Determine the overall shape of the cell, and ● distribute and support organelles within the cell.
Microfilaments	<ul style="list-style-type: none"> ● Strengthen and support the cell's surface; ● are involved in cell motility (A); and ● are responsible for cell shape changes (B and C).
Intermediate filaments	<ul style="list-style-type: none"> ● Resist pulling forces (tension) on the cell by acting like internal guy wires, and ● are part of anchoring junctions (D), which distribute tension throughout tissues.

A AMEBOID MOVEMENT

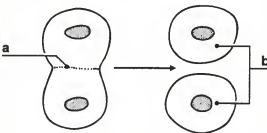
Microfilaments are involved in generating cell motility, such as that used by an amoeba (a) to travel.

**B CELL SHAPE CHANGES**

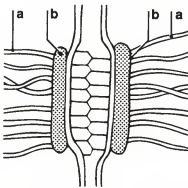
Microfilaments are responsible for changes in the shape of the cell membrane (a) that accompany endocytosis (secretion from the cell) (b), exocytosis (cell "eating") (c), and pinocytosis (cell "drinking") (d).

**C CYTOKINESIS**

At the end of cell division, a ring of microfilaments contracts at the dividing cell's equator. This forms a groove called the cleavage furrow (a) and eventually pinches the cell into two new daughter cells (b). This is called cytokinesis.

**D ANCHORING JUNCTION**

Intermediate filaments (a) are a major component of anchoring junctions between cells. They link the insides of a junction (b) to the opposite side of the cell membrane.



AMEBOID MOVEMENT

Ameboid movement is a specific type of cell motility that involves the creation of a pseudopodium (temporary projection or "false foot") to generate cell locomotion. It is used by:

- certain protozoan (unicellular) organisms such as ameba;
- the phagocytic ("engulfing" white blood cells) of vertebrates (animals with backbones); and
- other ameboid (shape-changing) cells found in animals.

ACTION

1 Inside an ameba or ameboid cell (a), its cytoplasm (semifluid mixture) (b) comprises fluid endoplasm and more-solid ectoplasm. In a stationary ameba, the endoplasm is found in the center and the ectoplasm is nearer the cell (plasma) membrane (c).

2 In order for the cell to move, the ectoplasm forms a small projection called a hyaline cap (d). The endoplasm flows forward into the hyaline cap and the projection becomes a pseudopodium (e).

3 As endoplasm reaches the end of the pseudopodium, it is converted into ectoplasm. As this ectoplasm flows back along the cell membrane, the stiff ectoplasmic outer tube of the pseudopodium is lengthened.

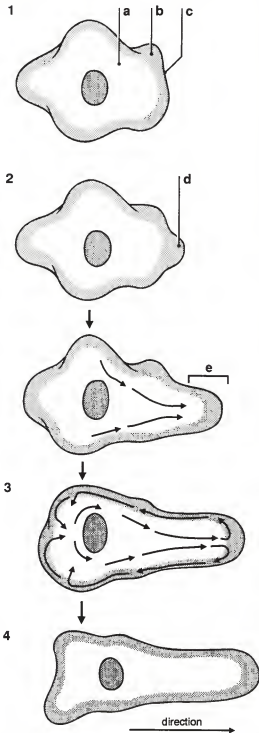
Simultaneously, the reverse is happening at the rear of the cell; the ectoplasm is converted into endoplasm and travels down the "tube" to the front of the ameba, bringing the rear forward.

4 In this way, the cell moves forward.

EXPLANATIONS

Microfilaments (tiny fibers) of the cell's cytoskeleton are involved in generating ameboid movement. It is not known exactly what their role is, however, although various theories have been proposed:

- The microfilaments fold up in the endoplasm and open out in the ectoplasm. This effectively squeezes the endoplasm forward.
- The microfilaments open out in the endoplasm and fold up in the ectoplasm. This pulls the endoplasm forward – the reverse of the above theory.
- The microfilaments slide against each other in a process similar to that involved in muscle cell contraction (see 3.45). This moves the endoplasm forward.
- The microfilaments disintegrate at the front and reassemble at the rear, taking the endoplasm with them.



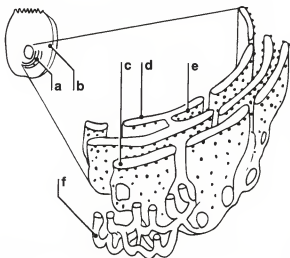
ENDOPLASMIC RETICULUM

LOCATION AND STRUCTURE

Endoplasmic reticulum (ER) (a) is an organelle (miniorgan) in a eukaryotic cell (b) – animal or plant, for example. ER is a network of fluid-filled tubes.

There are two types of ER, rough and smooth. A cell may have both or only one, depending on its function.

- **Rough ER** (c) is continuous with the nuclear membrane (d). Its external surface is studded with ribosomes (tiny, granular organelles) (e).
- **Smooth ER** (f) is continuous with rough ER, but does not have any ribosomes and is more tubular.



FUNCTIONS

Rough ER:

- Manufactures the building blocks of cell (plasma) membranes (phospholipids and cholesterol), and
- helps make and carry proteins.
- The external face provides a site for chemical reactions.

- 4 Completed proteins are encased in membranous vesicles (tiny membrane sacs) (g), which pinch off the ER and travel to other sites in the cell.

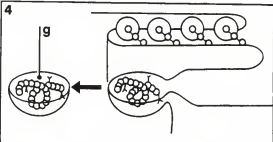
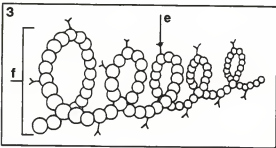
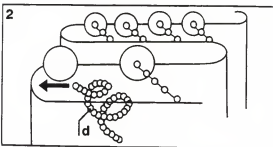
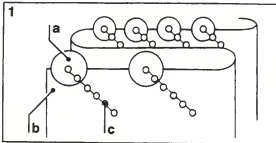
Protein synthesis and transport

- 1 Ribosomes (a) on the rough ER wall (b) manufacture protein strands (c).
- 2 The strands are folded within the tubes into the distinctive shapes identifying them as certain types of protein (d).
- 3 Sugars (e) may be added to proteins to form glycoproteins (f).

Smooth ER

Enzymes (biological catalysts) embedded in its membrane walls are involved with chemical reactions concerning:

- the making of cholesterol (a steroid);
- the making of sex hormones;
- the absorption, production, transport, and use of fats;
- the detoxification of drugs; and
- muscle cell contraction.



GOLGI APPARATUS 1: STRUCTURE

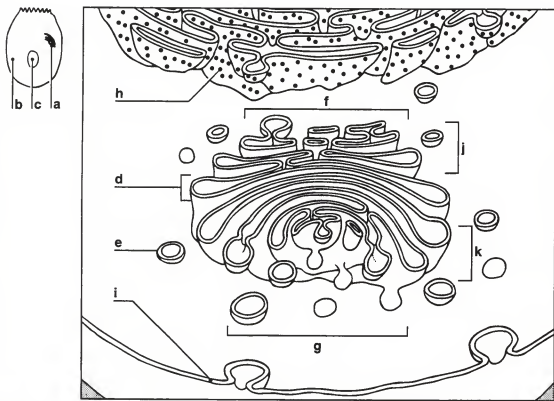
Camillo Golgi (1844–1926) was an Italian physician who discovered the apparatus in cells that now bears his name. It is now known to occur in all cells except bacteria.

STRUCTURE

The Golgi apparatus (a) is an organelle (miniorgan) found in cells (b). It is usually located near the nucleus (control center) (c). The number of these organelles may range from one in some animal cells to hundreds in some plant cells. In plant cells, the Golgi apparatus is usually more prominent and distinct than in animal cells.

- It is a stack of flat, membrane-enclosed, disk-shaped sacs known as cisternae (d). These cisternae are stacked like a pile of dinner plates.
- Surrounding each Golgi apparatus is a large number of membranous vesicles (tiny membrane sacs) (e).

- Each Golgi stack has two "faces" (sides): the *cis* face (f) is on one side and the *trans* face (g) is on the other. In general, the *cis* face looks toward the endoplasmic reticulum (another type of organelle) (h) and the *trans* face toward the cell (plasma) membrane (i). These faces are functionally and biochemically different, and contain quite different enzymes (biological catalysts).
- Each face is connected to its own network of branching and interconnected tubules (tiny tubes). These are known as the *cis*-Golgi network (j) and *trans*-Golgi network (k) respectively.



GOLGI APPARATUS 2: FUNCTIONS

The Golgi apparatus is believed to be the main routing director of proteins in the cell. It prepares and delivers proteins ready for:

- secretion from the cell;
- inclusion in lysosomes – bags of digestive enzymes;
- incorporation into the cell membrane; or
- incorporation into the cell wall of plant cells.

This preparation can include:

- the activation of proteins;
- the synthesis of complex sugars (polysaccharides) from simple sugars (monosaccharides); and
- the modification of proteins so that they can be recognized and directed to the right destination.

PROTEIN PREPARATION AND DELIVERY

1 Proteins and lipids (fats) (a) are delivered to the *cis* face (b) of the Golgi apparatus (c) in transport vesicles (d) sent by the rough endoplasmic reticulum (rough ER) (e).

2 The vesicles fuse with the membranes of the *cis*-Golgi network (f).

3 Within the apparatus, the proteins are prepared or modified. For example, enzymes may "cut" them at specific amino acid (protein building block) sequences to activate them.

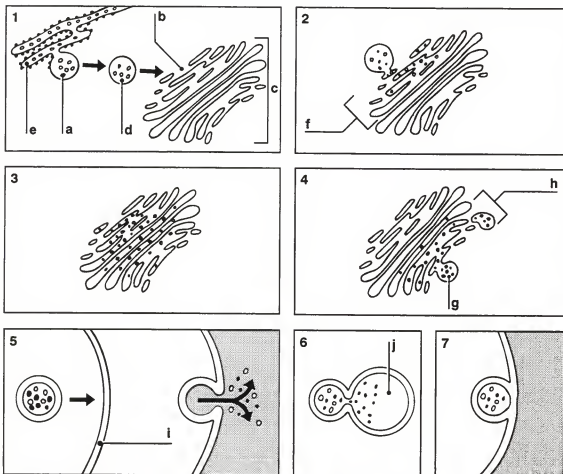
4 The proteins are then packaged into Golgi

vesicles (g). The vesicles pinch off from the *trans*-Golgi network (h) and migrate to other sites.

5 Vesicles containing proteins for secretion migrate to the cell membrane (i), where they are ejected by a process called exocytosis.

6 Vesicles containing enzymes might fuse with lysosomes (j).

7 Other vesicles containing cell membrane or, in plant cells, cell wall components fuse with the cell membrane, or cell wall.



LYSOSOMES

STRUCTURE

Lysosomes are a type of organelle (miniorgan) found in eukaryotic cells – plant or animal, for example. They are generally round, single-membrane sacs suspended in the cell's cytoplasm (semifluid mixture). Lysosomes contain many different digestive enzymes (biological catalysts) and have an internal pH of 5 (acidic). The number of lysosomes in a cell varies from one to several hundred; they are especially prevalent in phagocytes ("engulfing" white blood cells).

FUNCTIONS

Lysosomes:

- break down glycogen (stored energy);
- destroy injured, redundant, or harmful tissues and cells by releasing their enzymes – a process known as autolysis (cell self-destruction); and
- provide sites where substances (for example, bacteria, poisons, cellular debris, and malfunctioning organelles) can be safely digested or destroyed within the cell.
- The lysosome membrane has transport proteins through which the products of

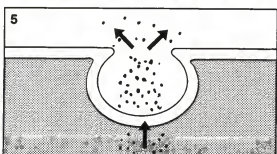
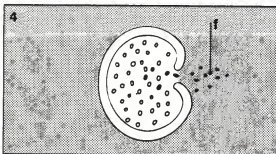
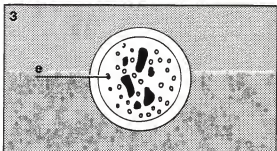
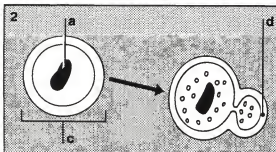
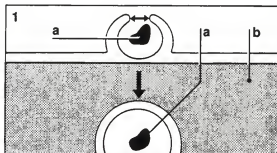
digestion – such as amino acids (protein building blocks), sugars, and nucleotides (nucleic acid building blocks) are returned to the cytoplasm. These products may be recycled or excreted.

The plant lysosome also:

- helps to produce turgidity (swelling) in the plant to prevent wilting; and
- acts as a storage depot for nutrients, nongerminating seeds, and waste products.

A LYSOSOME AT WORK

- 1 The particle (a) enters the cell (b) by a process such as phagocytosis (cell "eating").
- 2 The phagocytic vacuole or membranous vesicle (c) formed fuses with a lysosome (d).
- 3 The enzymes (e) in the lysosome digest the particle.
- 4 The resulting waste products (f) are secreted into the cell.
- 5 The wastes are expelled from the cell by exocytosis.

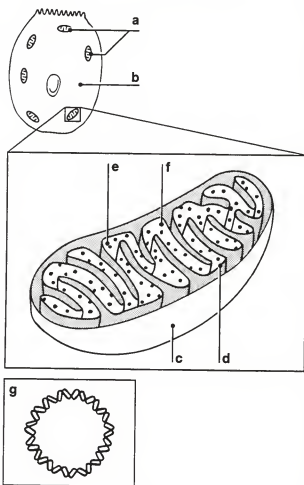


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MITOCHONDRIA

LOCATION AND STRUCTURE

- Mitochondria (a) are membrane-bound organelles (miniorgans) inside a eukaryotic cell (b) – plant or animal, for example. These mobile organelles are scattered throughout the cytoplasm (semifluid mixture).
 - Mitochondria are often depicted as sausage shaped, rod shaped, or spherical, depending on which organism the example is from. In a living cell, however, they are constantly changing shape. Each mitochondrion has:
 - c a smooth outer membrane;
 - d an inner membrane heavily folded into cristae (shelflike structures);
 - e a matrix (gel-like substance inside the inner membrane);
 - f enzymes (biological catalysts) dissolved in the matrix and embedded in the cristae; and
 - g its own genome (complete set of genes). This mitochondrial DNA (deoxyribonucleic acid), or mtDNA, is usually circular and double-stranded.
- In sexually-reproducing organisms, the mitochondrial genome is derived only from the female.



OVERVIEW OF FUNCTIONS

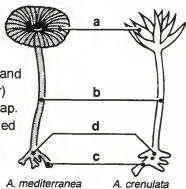
The main function of mitochondria is energy production by cellular respiration. This is basically the breakdown of glucose (a sugar) to produce the chemical-energy storage molecule ATP (adenosine triphosphate). Their heavily-folded inner membrane increases the surface area for manufacturing ATP.

FEATURES

- Mitochondria can fuse with each other and then separate.
- They are most concentrated in areas in which energy expenditure is greatest.
- Cells that consume a great deal of energy have many hundreds, perhaps thousands, of mitochondria. Cells that use less energy have fewer mitochondria.
- The number of mitochondria in a cell changes according to need. If, for instance, a resting muscle is repeatedly stimulated to contract, the number of mitochondria in its cells will increase. This increase can be up to ten-fold.
- Mitochondria will often attach themselves to contractile proteins such as actin myofibrils in a muscle cell, or inside the flagellum ("tail") of a sperm.
- A mitochondrion always arises from a previous mitochondrion. They replicate in the same way that bacteria do – by binary fission (simple division).
- Various muscle diseases are caused by mutations in mtDNA.

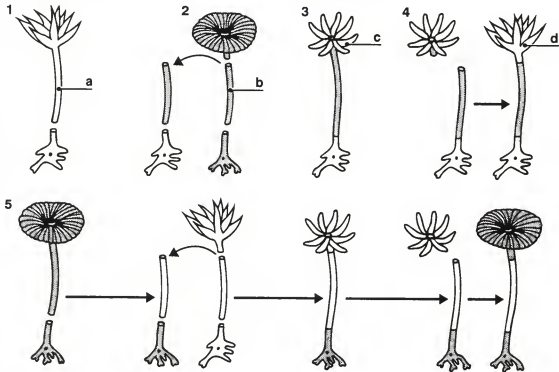
JOACHIM HAMMERLING'S WORK ON THE ROLE OF THE NUCLEUS

Joachim Hammerling (born 1901) was a German biologist. His principal contribution to cell biology was made in 1953 in the course of a series of experiments on a marine alga called *Acetabularia*. These are relatively large, unicellular organisms. Each consists of a cap (a), a stalk about 4-cm (1.5-in.) long (b), and a "foot," (or base) (c), which contains the nucleus (control center) (d). One species of this genus, *A. mediterranea*, has a circular cap. Another species, *A. crenulata*, differs only in that the cap is divided into many leaflike parts. If the cap is removed, a new one is generated. Hammerling's classic experiment involved these two *Acetabularia* species. For convenience, Hammerling described these, respectively, as "med" and "cren."



- 1 He cut off the stalk and cap of a cren (a).
- 2 He then grafted a med stalk (b) onto the cren base.
- 3 Eventually, a new cap (c) grew. This had features intermediate between those of the two normal caps.

- 4 He cut off this cap. When a second cap (d) grew, it was identical to a normal cren cap.
- 5 Hammerling repeated the experiment in reverse. A med base created a med cap, even if a cren stalk had been grafted on to the med base.



Hammerling concluded that:

- Chemicals produced by the nucleus had traveled through the cytoplasm (semifluid mixture) to carry out the regeneration.
- The first cap had intermediate qualities as chemicals from the absent nucleus that were present in the grafted stalk affected the regeneration.
- By the time the second cap was produced, these chemicals had been used up. So the regeneration was solely under the control of the present nucleus.

This confirmed that the features of the individual cell were determined by the nucleus. Hammerling had shown that the nucleus was a "blueprint" for the organism.

NUCLEUS 1: STRUCTURE

The nucleus (control center) is the largest, most important organelle (miniorgan) found in cells. All eukaryotic (such as plant or animal) cells have a nucleus. One exception is the mature red blood cell of vertebrates (animals with backbones). The red blood cell is nucleated at an early stage of development, but then ejects its nucleus and becomes largely a vessel for hemoglobin (a blood protein). Prokaryotes (bacteria) are not considered to possess "true" nuclei, as their equivalent structures are not enclosed by a membrane.

STRUCTURE

- The eukaryotic ("true") nucleus (a) is usually placed centrally in a cell (b).
- Its shape often reflects the shape of the cell. For example, flat cells have flat nuclei.
- Some protozoan (unicellular) organisms have two nuclei per cell: a micronucleus concerned with sexual reproduction and a macronucleus (or meganucleus) concerned with asexual functions. In animals, some muscle cells have more than one nucleus.

A nucleus consists of:

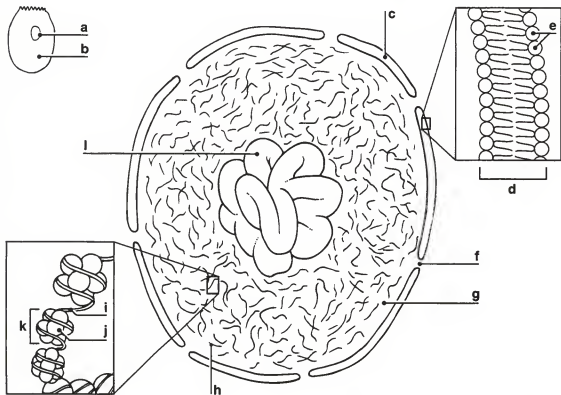
- c **The nuclear envelope** This is a double nuclear membrane. Each nuclear membrane consists of a phospholipid bilayer (d) – two layers of phospholipid molecules (e).
- f **Nuclear pores** At certain points, the nuclear membranes fuse to form holes in the nuclear envelope.

g **Nucleoplasm** This is a gel-like fluid containing vital chemicals, such as nutrients and salts. The nucleolus and chromatin are suspended in the nucleoplasm.

h **Chromatin** Strands of DNA (deoxyribonucleic acid) (i) wound around histone proteins (j) comprise chromatin fibers. A clump of eight histones on a DNA strand comprises one nucleosome (k).

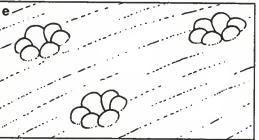
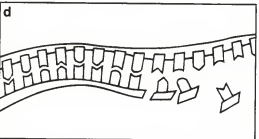
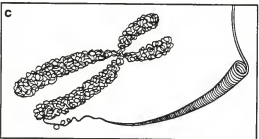
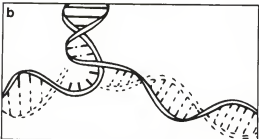
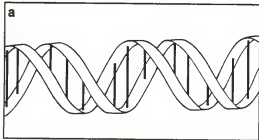
Normally, chromatin is not visible under a light microscope. During cell division, however, chromatin condenses to form chromosomes, which are visible under a light microscope.

i **The nucleolus** This is a compact ball of RNA (ribonucleic acid) and proteins. It does not have an outer membrane. Every nucleus has one or more nucleoli.



NUCLEUS 2: FUNCTIONS

The nucleus regulates and coordinates all of the cell's activities.



INHERITANCE

- The nucleus is the region in which the genetic (inherited) material of the cell – DNA (deoxyribonucleic acid) (a) – is stored. This information tells the cell how to produce proteins (the building blocks of life).
- Prior to cell division, the nucleus accurately duplicates its DNA (b) so that each daughter cell can receive an identical genome (complete set of genes).
- During cell division, chromatin fibers coil up again and again to produce chromosomes (c). These enable the distribution of genetic material to the new daughter cells.

GENE EXPRESSION

- The nucleus is the site of RNA (ribonucleic acid) synthesis (d):
- DNA acts as a template ("mold") to create mRNA (messenger RNA), and
- rRNA (ribosomal RNA) is made by the nucleolus. rRNA leaves the nucleus to become ribosomes (tiny, granular particles).
- mRNA and ribosomes are vital to the process of expressing genes – creating proteins from them.
- Histones play an important role in gene regulation. Changes in the shape of these proteins can, for example, expose different genes and alter the protein synthesis process.

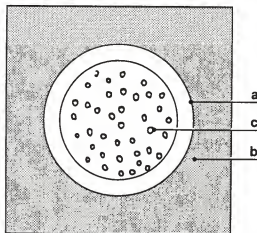
TRANSPORT OF SUBSTANCES

- The relatively large nuclear pores (e) make the nuclear membrane semipermeable. This allows the free passage of molecules that need to be imported or exported by the nucleus.

PEROXISOMES

STRUCTURE

Peroxisomes (a) are a type of organelle (miniorgan) found in eukaryotic cells – plant or animal, for example. They are single-membrane sacs suspended in the cell's cytoplasm (semifluid mixture) (b). Peroxisomes are very similar to lysosomes (see 3.29), but tend to be smaller. They contain powerful enzymes (biological catalysts) (c). The number of peroxisomes in a cell varies from one to several hundred. They are especially prevalent in the liver and kidney cells of animals. Peroxisomes are formed by growth and binary fission (simple division) of other peroxisomes.



FUNCTIONS

- Peroxisomes detoxify harmful and poisonous substances such as alcohol, hydrogen peroxide, and formaldehyde.
- Peroxisomes disarm dangerous free radicals. These are chemicals with unpaired electrons. They can scramble the structure of vital compounds such as DNA

(deoxyribonucleic acid), proteins, and lipids (fats).

- Peroxisomes also break down fatty acids. Although free radicals and hydrogen peroxide are natural by-products of cell activities, if they accumulate to certain levels they can be very harmful.

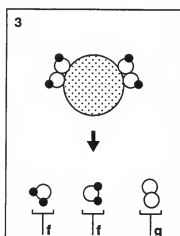
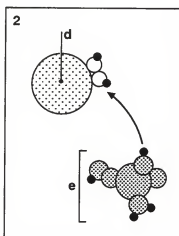
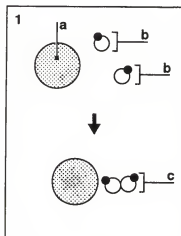
Detoxification

Peroxisomes use the oxidase (oxygen-using) enzymes peroxidase and catalase to detoxify substances.

- 1 Peroxidase (a) disarms substances such as hydroxyl ($\cdot\text{OH}$) free radicals (b) by converting them to hydrogen peroxide (H_2O_2) (c).

- 2 Catalase (d) uses the hydrogen peroxide to oxidize other harmful substances (e).

- 3 When excess hydrogen peroxide accumulates, catalase breaks the surplus down to water (H_2O) (f) and molecular oxygen (O_2) (g).



Key:

- Peroxidase Oxygen atom
 Catalase Hydrogen atom

RIBOSOMES

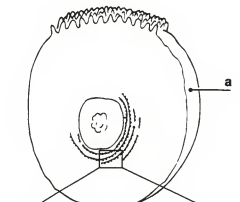
LOCATION AND STRUCTURE

A Ribosomes are organelles (miniorgans) found inside a eukaryotic cell (**a**) – plant or animal, for example. They look like tiny, round granules.

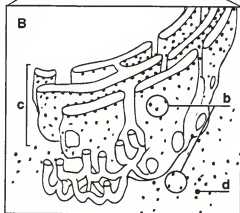
B Ribosomes (**b**) are either attached to the rough endoplasmic reticulum (rough ER, a network of fluid-filled tubes and channels) (**c**) or suspended freely in the cell's cytoplasm (semifluid mixture) (**d**).

C Ribosomes have two parts, a large (**e**) and a small (**f**) subunit. They are made of rRNA (ribosomal ribonucleic acid) and proteins. Each ribosome is just over 20 nm in diameter and 30nm in height.

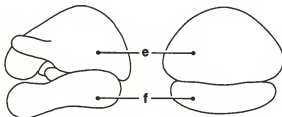
A



B



C



side view

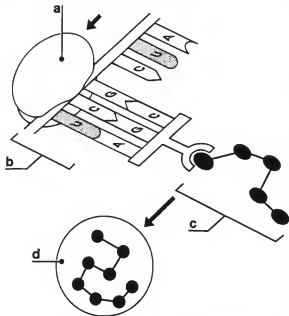
front view

FUNCTIONS

Ribosomes are involved in protein synthesis. A ribosome (**a**) is the site at which mRNA (messenger RNA) (**b**) is translated into the amino acid sequence (**c**) of a protein (**d**). The same strand of messenger RNA can be used for the synthesis of a large number of identical protein molecules.

Depending on the task it needs to carry out, each ribosome can be either bound or free.

- **Free ribosomes** (those not attached to rough ER) are involved in making proteins to be used by the cell.
- **Membrane-bound ribosomes** (those attached to rough ER) are mostly involved in making proteins that will be used in the cell membrane or exported out of the cell.



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NERVE CELLS

In complex animals, nerve cells form the organs of the central nervous system (CNS) – the brain and spinal cord – and peripheral nervous system (PNS), which comprises nerves and nerve processes (extensions) that connect the CNS to muscles, glands, and receptors.

NEURONS

Structure

Nerve cells are called neurons. They do not go through the process of reproducing themselves (mitosis). Neurons are said to be amitotic: if destroyed, they cannot be replaced. Ganglia are collections of nerve-cell bodies outside the CNS. All neurons contain the same elements:

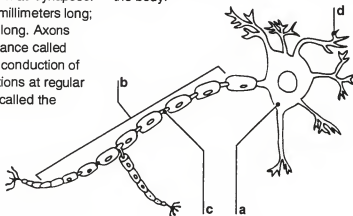
a Cell body This includes a nucleus (control center) and extensions called processes.

b Axon This is a long, slim "trunk" that transmits information from the cell body to other cells via junctions known as synapses. Some axons are only a few millimeters long; others are more than a yard long. Axons are sheathed in a fatty substance called myelin, which helps with the conduction of electrical impulses. Constrictions at regular intervals along the axon are called the nodes of Ranvier (**c**).

d Dendrites These are networks of short fibers that branch out from the axon or cell body and link the ends of axons from other neurons. Dendrites are the cell's receivers of information, bringing signals to their neuron's own cell body. Each neuron might have hundreds of dendrites.

Functions

Neurons communicate electrochemically with one another to transmit impulses throughout the body.



NEUROGLIA

The nervous system also contains neuroglia cells. These do not conduct nerve impulses. Instead, they support and protect neurons. They are capable of mitosis (so if damaged can be replaced). There are four types of neuroglia within the CNS:

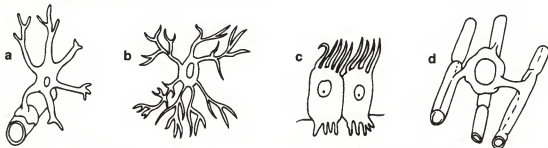
a star-shaped astrocytes cling to neurons and help protect them;

b smaller microglia are spider shaped and help

to get rid of dead brain cells and bacteria;

c ependymal cells line the ventricles of the spinal cord and brain, and their cilia (hairlike fronds) help circulate cerebrospinal fluid; and **d long-extended oligodendrocytes** wrap around and protect nerve fibers.

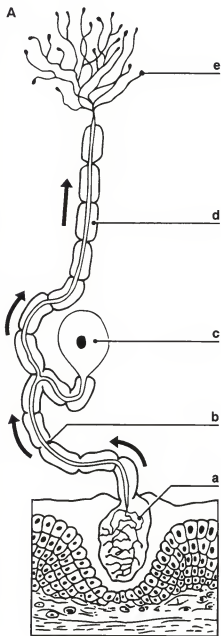
Sometimes, Schwann cells and satellite cells, found in the PNS, are considered neuroglia.



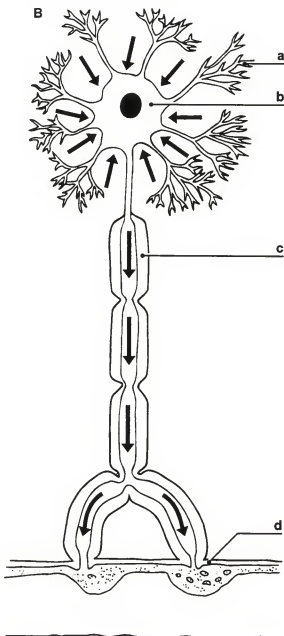
HOW NERVE CELLS WORK

A SENSORY NEURONS

Sensory neurons (or receptor cells) are nerve cells that convey information *from* receptors in the body to the central nervous system (CNS), which comprises the brain and spinal cord. Dendrites (short projections) (a) in the skin, eye, nose, etc., pick up signals. These are then transmitted as nerve impulses along the axon (cell "trunk") (b) to the cell body (c). Another axon (d) conveys the impulses to nerve endings (e) in the brain or spinal cord.

**B MOTOR NEURONS**

Motor neurons are nerve cells that convey information *from* the CNS to muscles and glands. Electrical impulses in a motor neuron travel in the opposite direction from those in a sensory neuron. Dendrites (a) collect signals from nerve fibers in the brain or spinal cord. These are transmitted to the cell body (b) and via an axon (c) to motor end plates (d), which stimulate glands to secrete substances or muscle cells to contract, for example.



TYPES OF NEURONS

NEURONS BY FUNCTION

Neurons (nerve cells) are grouped here according to whether they send information *to* or *from* the central nervous system (CNS) – the brain and spinal cord – or peripheral nervous system (PNS) – nerves and nerve processes that connect the CNS to muscles, glands, and receptors.

NEURON	STRUCTURE	FUNCTION
Afferent (sensory neuron)	<ul style="list-style-type: none"> ● cell body located in PNS ● short axon ("trunk") extending into CNS ● longer dendrites (projections) located in the PNS 	<ul style="list-style-type: none"> ● Brings signals to the CNS <i>from</i> elsewhere in the body.
Efferent (motor neuron)	<ul style="list-style-type: none"> ● cell body located in CNS ● long axon extending into PNS ● short dendrites located in CNS 	<ul style="list-style-type: none"> ● Sends out signals <i>from</i> the CNS to the body.
Interneuron	<ul style="list-style-type: none"> ● short or long axon located in CNS ● short dendrites located in CNS 	<ul style="list-style-type: none"> ● Transmits impulses <i>between</i> afferent and efferent neurons.

NEURONS BY STRUCTURE

A Multipolar neurons

These are the most common type of neuron. They have multiple (three or more) processes (axons and dendrites) projecting from the cell body and are found everywhere in the CNS. Although most have one axon and many dendrites, there are some that have only dendrites.

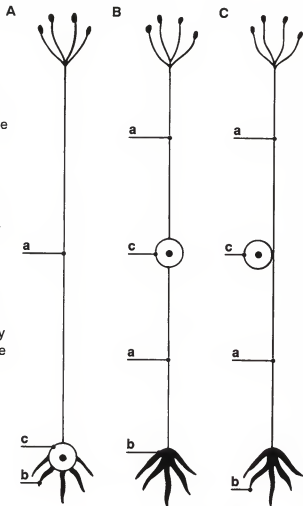
B Bipolar neurons

These have one process (a dendrite) leading into the cell body and another process (the axon) leaving it. This type of neuron is mostly found in the retina of the eye.

C Pseudounipolar neurons

Pseudounipolar neurons originate as bipolar neurons, but during development their two processes fuse to form a single process. They are found in a chain of ganglia (group of nerve cells located outside the CNS) that runs parallel to the spinal cord.

Key:
a Axon
b Dendrite
c Cell body



NERVE IMPULSES

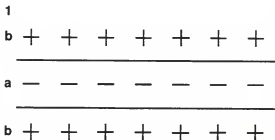
In complex animals, messages are sent around the body and to and from the brain by electrical impulses transmitted via nerves. Nerves emit impulses when stimulated by a physical, chemical, or electrical event that alters the cell (plasma) membrane for a short time. The size of a cell's axon ("trunk") affects the speed with which it conducts an impulse. Small axons conduct impulses at around 1 mph, while large axons can transmit impulses at 270 mph.

1 RESTING NEURON

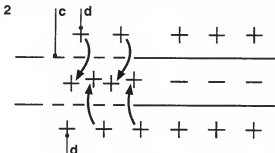
A resting neuron (nerve cell) is negatively charged inside the cell membrane (a) and positively charged outside the cell membrane (b). This is called the resting membrane potential. It is maintained by:

- the differential permeability of the cell membrane to sodium and potassium ions – sodium diffuses into the cell more slowly than potassium diffuses out of the cell; and
- the sodium-potassium pump (see 3.12), which drives more positive ions out of the cell than it drives in.

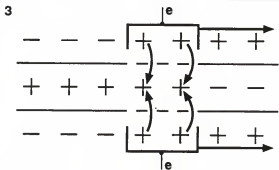
As a result, more positive ions collect on the outside of the cell membrane than on the inside.

**2 STIMULATED NEURON**

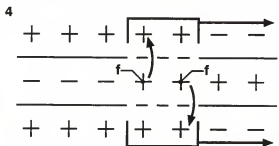
When a neuron is stimulated, the permeability of a patch (c) on the cell membrane alters. Positively charged sodium ions (d) begin to enter the cell, making the inside locally positive. This is called depolarization.

**3 THE NERVE IMPULSE**

Depolarization spreads along the cell membrane (e). Eventually, the charge on either side of the cell membrane is temporarily reversed. This is called reverse polarization. It is, in fact, the nerve impulse traveling along the cell membrane.

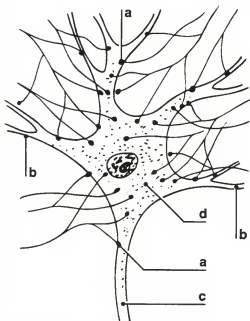
**4 REPOLARIZATION**

The cell membrane alters its permeability again. Positively charged sodium ions begin to pass out of the cell (f). Finally, the outside of the cell is again positively charged, and the inside negatively charged. This is called repolarization.



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SYNAPSES



Synapses are specialized communication junctions that occur between neurons (nerve cells) and between neurons and muscle or gland cells. Tiny feet called synaptic buttons (a) at the end of each synapse attach to the dendrites (b), axon (c), and cell body (d) of the next cell.

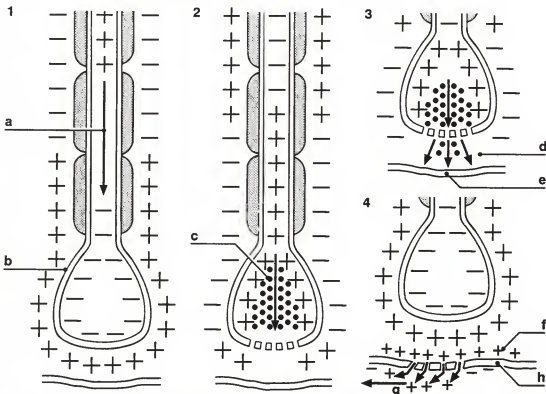
NEUROTRANSMITTERS

Neurotransmitters are chemical messengers that permit the transfer of an electrical impulse from one cell to the next. They "leap" from the synaptic buttons of one neuron to the axon or dendrites of another by diffusing across the gap. Chemicals that allow an impulse to flow through a neuron are called excitatory neurotransmitters. Inhibitory neurotransmitters block electrical impulses. Many drugs that act on the brain and nervous system either act like neurotransmitters or block their action.

HOW THE SYNAPSE WORKS

- 1 A nerve impulse (a) arrives at the synaptic button (b) of a synapse.
- 2 A neurotransmitter (c) is released.
- 3 The neurotransmitter quickly diffuses across the gap (d) and its molecules fit into receptors on the other surface (e).
- 4 This changes the local permeability of the

target cell membrane to sodium, and positive sodium ions (f) pass in causing the surrounding area to reverse its electrical charge and undergo depolarization. As a result, a nerve impulse (g) is triggered in the second neuron (h).



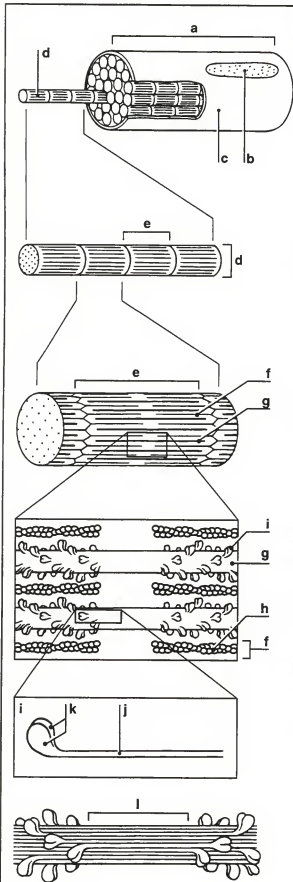
TYPES OF MUSCLE FIBERS

All animals except the most simple have muscles. Muscle cells are called fibers. There are three types of muscle fibers: skeletal, cardiac, and smooth. They all share the ability to contract (or shorten).

CELL TYPE	CELL DESCRIPTION	TISSUE DESCRIPTION	LOCATION	FUNCTIONS	NATURE OF CONTROL
Skeletal	Long, cylindrical cells (a) with many nuclei (contol centers) (b) near the cell (plasma) membrane. Cells are striated (banded by light and dark contractile proteins) (c).	Cells collected into bundles and covered by connective tissue form individual muscles.	<ul style="list-style-type: none"> ● attached to bones ● attached to eyeballs ● upper two-thirds of esophagus (gullet – tube leading to stomach) ● occasionally attached to skin 	<ul style="list-style-type: none"> ● Provides movement of body parts (for example, limbs, facial features, and eyes). 	Mainly voluntary (under conscious control).
Cardiac	Striated, cylindrical cells (a) with branches (b) and one central nucleus (c).	Cells are separated by intercalated disks (junctions unique to cardiac muscle) (d) to form a dense network encased in connective tissue.	<ul style="list-style-type: none"> ● walls of heart 	<ul style="list-style-type: none"> ● Produces rhythmic contractions (heartbeats) that propel blood into circulation. 	Involuntary (not under conscious control).
Smooth	Unstriated, spindle-shaped (long with tapering ends) cells (a) with one central nucleus (b).	Cells are arranged close together into sheets. These sheets may be layered at right angles to each other to form the muscle tissue.	<ul style="list-style-type: none"> ● walls of hollow organs of the digestive, respiratory, and urinary tracts ● uterus ● blood vessels ● within eye ● attached to hairs 	<ul style="list-style-type: none"> ● Move substances along internal passageways using propulsion; ● produce uterine contractions; ● change width of blood vessels; ● change pupil diameter and lens shape; and ● erect hairs. 	Involuntary.

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MUSCLE FIBERS 1: STRUCTURE



MUSCLE FIBERS

- Muscle cells are called muscle fibers (a). They are tubular and can be up to 3 cm (1.18 in.) long and one-tenth of a millimeter wide.
- Muscle fibers have many nuclei (control centers) (b). A muscle fiber is therefore said to be a syncytium.
- The fibers are surrounded by endomysium (a delicate sheath of connective tissue) (c).
- Each muscle fiber comprises many myofibrils (d).

Myofibrils

- A myofibril (d) is a rodlike structure that has the ability to contract (shorten) when stimulated. This makes muscle fibers excitable cells (ones that react to a stimulus).
- Myofibrils comprise special contractile sections called sarcomeres (e).

Sarcomeres

- Sarcomeres can only be resolved using electron microscopes. A sarcomere (e) is made up of two kinds of filament: thin (actin) filaments (f) and thick (myosin) filaments (g). These are known as myofilaments.

Myofilaments

- Thin (f) and thick (g) myofilaments are made up of proteins called contractile proteins.
- Thin filaments contain actin molecules (h).
- Thick filaments contain myosin molecules (i).

Myosin molecules

- Each myosin molecule (i) has a long "tail" (j) and two "heads" (or cross bridges) (k), which protrude from the filament.
- The myosin tails form the central part (l) of a thick filament. This part of the filament is free of myosin heads.

MUSCLE FIBERS 2: SKELETAL MUSCLE FIBERS**TYPES**

There are three types of skeletal muscle fibers: red/slow, red/fast, and white/fast. They differ in their abilities to contract and in their resistance to fatigue. These factors are determined by the capacity of the fiber to make ATP (adenosine triphosphate), the fuel with which cells work.

Red/slow fibers

- These fibers are small and have many capillaries.
- They contain a special pigment (myoglobin) that stores oxygen and facilitates its use within the cell. Myoglobin also makes the muscle fiber appear red. Cells that are especially good at using oxygen are said to have an aerobic metabolism.
- Red/slow fibers also have many mitochondria (energy-producing miniorgans). They are designed for endurance and contract slowly but do not produce much power.
- They have a relatively low store of glycogen (fuel).

Red/fast fibers

- These fall in between red/slow fibers and white/fast fibers (*see table below*).

White/fast fibers

- These are found in muscles that are used for rapid bursts of energy.
- They are larger than red/fast cells, have little myoglobin, few mitochondria, and few capillaries.
- They appear white in color.
- White/fast fibers have a large store of glycogen and can produce ATP very quickly, but they fatigue rapidly.
- They do not rely on oxygen in order to function and so are said to be anaerobic.

		RED/SLOW	RED/FAST	WHITE/FAST
STRUCTURE	Color	red	pink	white
	Diameter of fiber	small	intermediate	large
	Number of capillaries	many	many	few
	Mitochondria	many	many	few
	Myoglobin content	high	high	low
ENERGY	Glycogen stores	low	intermediate	high
	Energy system used	aerobic	aerobic	anaerobic
REACTION	Speed of contraction	slow	fast	fast
	Resistance to fatigue	high	intermediate	low

LOCATION OF FIBER TYPES

Different types of skeletal muscle fibers are found in different parts of the body. In humans, for example, muscles that control posture (mainly in the back), are constantly active and must therefore be slow to fatigue.

They contain a large proportion of red/slow fibers. Muscles in the arms contain a large proportion of white/fast fibers because they are needed to produce strong contractions over short periods of time.

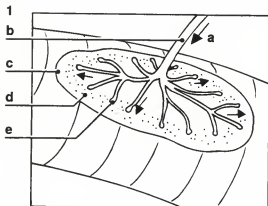
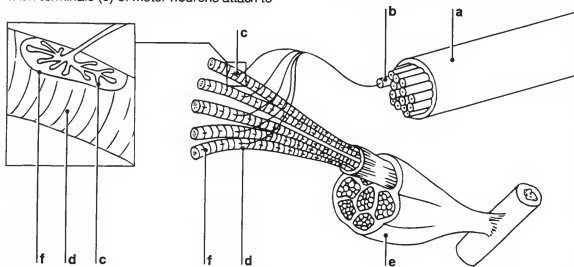
MUSCLE FIBERS 3: CONTRACTION (1)**MOTOR UNITS**

Muscle fibers have to contract quickly when stimulated in order to bring about a given action. To do this they are fed by nerves from the central nervous system – the brain and spinal cord. A single neuron (nerve cell) and all the muscle fibers that it stimulates are known as the motor unit. Different muscles have a different number of motor units. The number of muscle fibers within a motor unit varies from as few as four to many hundreds. Muscles that require very precise action have small motor units. Muscles with less precise movements have large motor units.

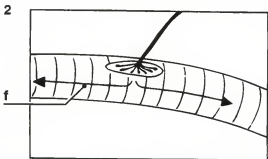
Structure

Each motor unit is served by one motor nerve (a) housing many motor neurons (b). The axon terminals (c) of motor neurons attach to

muscle fibers (d) in the muscle (e) at points on the muscle fiber called motor end plates (f).

**HOW A MOTOR UNIT WORKS**

- 1 A nerve impulse (a) is sent out along the motor neuron (b). When the impulse arrives at the end plate (c), a chemical called acetylcholine (d) is released from the axon terminals (e).
- 2 This crosses the gap and stimulates the end plate of the muscle fiber in the form of an electric charge. The electric charge passes along the muscle, which contracts. The muscle fiber (f) relaxes unless there is another nerve impulse.

**The all-or-none principle**

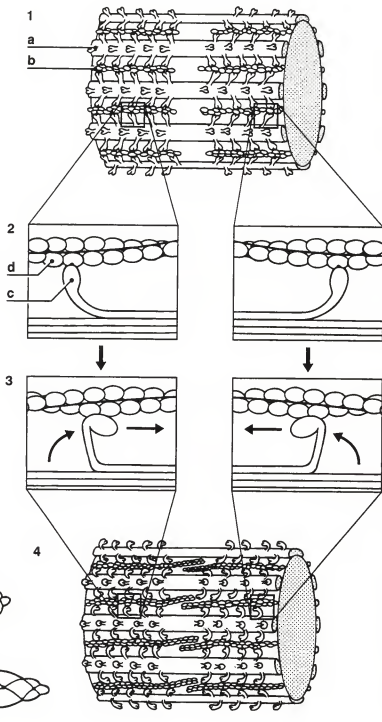
A single muscle fiber does not act with graded responses as the power of the stimulus increases. It either responds maximally or it does not respond at all. This means that the force of contraction of the muscle as a whole is dependent upon the number of fibers that the stimulus excites. A strong stimulus excites more fibers than does a weak one.

MUSCLE FIBERS 4: CONTRACTION (2)**SLIDING FILAMENT THEORY**

Muscles fibers comprise microscopic structures called myofibrils. These are made of sections called sarcomeres, which contain thick and thin segments called myofilaments. According to the sliding filament theory, proposed in 1954 by Hugh Huxley (born 1924), a muscle contracts when the myofilaments slide across each other. The process is powered by ATP (adenosine triphosphate) – the chemical-energy storage molecule.




CONTRACTION

- 1 When a muscle fiber is stimulated by the nervous system, the thick (a) and thin (b) filaments within a sarcomere become linked.
- 2 Each link is formed when a myosin head (or cross bridge) (c) of a thick filament locks onto the actin (d) of a thin filament.
- 3 The cross bridges pull the thin filaments toward the center of the sarcomere. Each cross bridge does this several times during a contraction.
- 4 The resulting overlapping of the thin filaments causes the sarcomere to shorten.
- 5 The tiny amount of shortening of each sarcomere is multiplied by the large number of sarcomeres in each fiber. The muscle fiber itself shortens to about two-thirds of its resting length.



TYPES OF BLOOD CELLS 1

Blood occurs in vertebrates (animals with backbones). It is composed of roughly 55% plasma (watery fluid) and 45% blood cells, including platelets.

CELL TYPE	STRUCTURE AND FUNCTIONS	NUMBER PER mm ³ OF BLOOD	LIFE SPAN
ERYTHROCYTES (red blood cells)	Structure Red blood cells are biconcave disks. They do not have a nucleus (control center) nor any organelles (miniorgans). They are filled with hemoglobin, an iron-containing protein with a high affinity for oxygen. This gives them a pale red color.	4–6 million	100–200 days (120 average)
 <p>7–8 μm diameter</p> <p>side view</p>	Functions Transport oxygen and carbon dioxide around the body.	Percentage of total blood composition: 45% 	Percentage of total blood cells: 98% 

LEUKOCYTES (white blood cells) comprise less than 1% of total blood composition

Granulocytes

Neutrophils
(or polymorphs)

Structure
Neutrophils are ameboid (shape-changing) cells with multilobed nuclei of up to six segments joined by narrow strands. They contain many large lysosomes, mitochondria, a Golgi apparatus, and endoplasmic reticulum (ER) – all types of organelles.

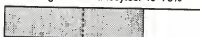
3,000–7,000 6 hrs–few days



10–14 μ m diameter

Functions
They are phagocytes – they engulf bacteria, harmful substances, and debris.

Percentage of all leukocytes: 40–70%



Eosinophils



10–14 μ m diameter

Structure
Cells with nuclei that have two prominent lobes joined by a thin strand. They are packed with lysosomes.

100–400 8–12 days

Functions
● Kill parasitic worms, and
● counteract allergic reactions.

Percentage of all leukocytes: 1–4%



Basophils



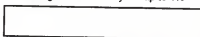
10–12 μ m diameter

Structure
Similar to eosinophils.

20–50 few hrs–few days

Functions
Probably related to allergic reactions as they release histamine and heparin – an anticoagulant (anticlumping agent).




Percentage of all leukocytes: up to 1%



(continued on 3.47)

TYPES OF BLOOD CELLS 2

(continued from 3.46)

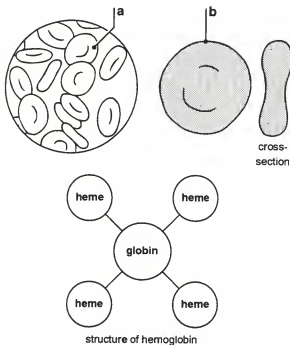
CELL TYPE	STRUCTURE AND FUNCTIONS	NUMBER PER mm ³ OF BLOOD	LIFE SPAN
LEUKOCYTES (white blood cells) (continued)			
Agranulocytes			
Lymphocytes	<p>Structure</p> <p>Lymphocytes have a large, dense-staining nucleus with a thin rim of cytosol (gel-like fluid). They fall into two main classes: T-cells and B-cells.</p> <p>Functions</p> <p>Along with monocytes, lymphocytes are the main cells of the immune system. They:</p> <ul style="list-style-type: none"> ● produce antibodies, and ● assist with the immune response. 	1,500–3,000	hrs–years
 5–17 μ m diameter		Percentage of total blood cells: 0.04%	
		Percentage of all leukocytes: 20–45%	
Monocytes (or macrophages)	<p>Structure</p> <p>Monocytes have a large solid-seeming nucleus with an indentation on one side, a prominent Golgi apparatus, many lysosomes, and abundant mitochondria. When present in the various tissues of the body, they are known as macrophages.</p> <p>Functions</p> <p>Along with lymphocytes, monocytes are the main cells of the immune system. They are actively phagocytic ("engulfing") cells that attack and destroy bacteria and other infecting organisms.</p>	100–700	months
 14–24 μ m diameter		Percentage of all leukocytes: 4–8%	
PLATELETS AND THROMBOCYTES	<p>Structure</p> <p>Platelets are not strictly cells. They are fragments of cells called megakaryocytes and do not have a nucleus. In vertebrates other than mammals, the equivalent cells are called thrombocytes; these do have a nucleus.</p> <p>Functions</p> <p>Platelets and thrombocytes assist in blood clotting.</p>	250,000–500,000	5–10 days
 2–4 μ m diameter		Percentage of total blood composition: less than 1%	
		Percentage of total blood cells: less than 2%	

© DIAGRAM

RED BLOOD CELLS 1: STRUCTURE AND OVERVIEW OF FUNCTIONS

STRUCTURE

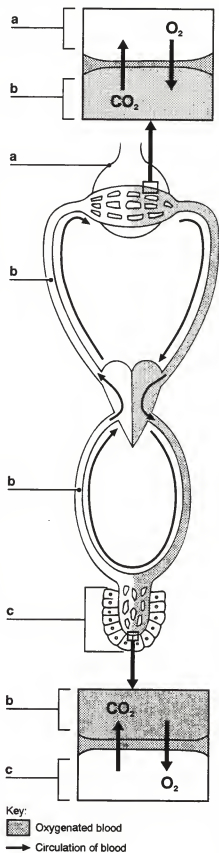
Erythrocytes (red blood cells) (a) are of very simple structure. They consist of little more than a cell (plasma) membrane (b), stiffened with internal proteins, and a protein filling. In shape, they are biconcave disks – they have two inwardly curving sides. When mature, erythrocytes have no nucleus (control center) nor organelles (miniorgans). The diameter of an erythrocyte is about $7\text{ }\mu\text{m}$ and it has a rim thickness of about $1.9\text{ }\mu\text{m}$. Erythrocytes are filled with hemoglobin, an iron-containing protein with a high affinity for oxygen. This gives red blood cells their pale red color.



FUNCTIONS

Erythrocytes are essential to life and health. This is because they are the vehicles that transport the vital gas oxygen (O_2) from the lungs (a) through the bloodstream (b) to all the cells of the body (c), and carry the harmful waste gas carbon dioxide (CO_2) from cells to the lungs, where it is expelled.

The structure of an erythrocyte reflects its main tasks. The lack of a nucleus and any organelles maximizes their carrying capacities. The erythrocyte cell membrane contains around 15 different classes of transmembrane proteins, which are vital in transporting molecules such as oxygen and carbon dioxide in and out of the cell.



RED BLOOD CELLS 2: TRANSPORT OF OXYGEN

Erythrocytes (red blood cells) and plasma (watery fluid) are the main components of blood involved in transporting the gases oxygen and carbon dioxide between the lungs and the tissue cells. The transport of these gases uses diffusion. This is the tendency for

substances to diffuse from an area where they are in higher concentration to one where they are in lower concentration.

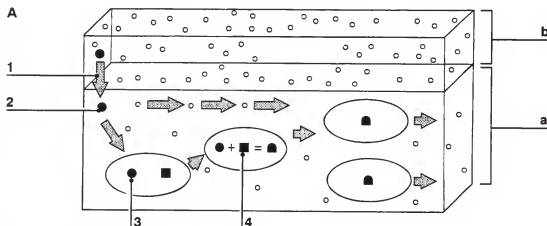
The process can be divided into two stages: the loading (picking up) and the unloading (dropping off) of the gases.

OXYGEN TRANSPORT**A Loading of oxygen**

- 1 Oxygen enters the blood (a) from the lungs (b) during respiration (breathing).
- 2 It then dissolves in the plasma (watery fluid).
- 3 Most of the oxygen will then diffuse from the plasma into the erythrocytes. (About 3%

remains in solution in the plasma.)

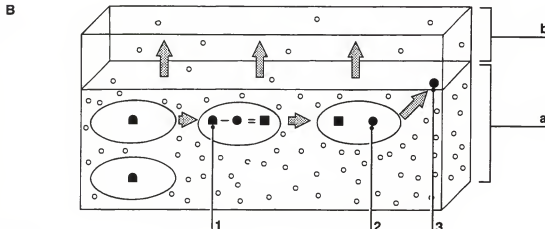
- 4 The oxygen combines with hemoglobin molecules in the erythrocytes to form a compound called oxyhemoglobin.

**B Unloading of oxygen**

- 1 When the blood (a) reaches the tissue cells (b), the bonds linking the oxygen and the hemoglobin break.

- 2 The oxygen can then diffuse back into the plasma.

- 3 The oxygen is then free to enter the tissue cells, which use it to make energy.



Key:

● Oxygen

■ Oxyhemoglobin molecule

■ Hemoglobin molecule

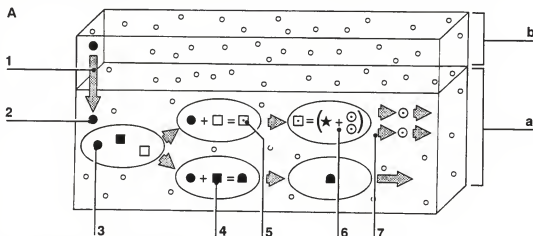
○ Erythrocyte

RED BLOOD CELLS 3: TRANSPORT OF CARBON DIOXIDE

CARBON DIOXIDE TRANSPORT

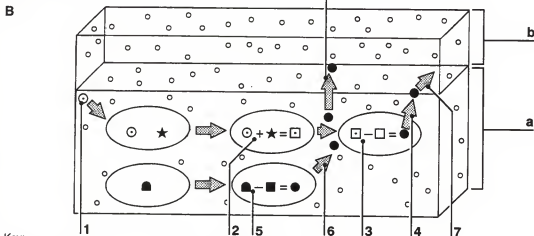
A Loading of carbon dioxide

- 1 Carbon dioxide enters the blood (a) from the tissue cells (b). This gas is produced by cells as a byproduct of metabolic processes.
- 2 Some of it then dissolves in the plasma.
- 3 More of the carbon dioxide diffuses into the erythrocytes.
- 4 Some of this carbon dioxide combines with hemoglobin in the erythrocytes to form a compound called carbaminohemoglobin.
- 5 Most of the carbon dioxide (about 70%) combines with water in the erythrocytes to form carbonic acid.
- 6 This acid then separates into its component hydrogen and bicarbonate ions.
- 7 The bicarbonate ions then diffuse out of the cell and into the plasma.



B Unloading of carbon dioxide

- 1 On reaching the lungs, the bicarbonate ions diffuse back into the erythrocytes.
- 2 The bicarbonate and hydrogen ions recombine into carbonic acid.
- 3 The carbonic acid separates into water and carbon dioxide.
- 4 The carbon dioxide then reenters the plasma (a) by diffusion.
- 5 Also, the bonds linking the carbaminohemoglobin break.
- 6 This carbon dioxide also diffuses back into the plasma.
- 7 From the plasma, the carbon dioxide is free to enter the air in the lungs (b) and be expelled during breathing.



Key:

- Carbon dioxide
- Hemoglobin molecule
- Water
- ⬡ Carbaminohemoglobin
- ★ Hydrogen ion
- Bicarbonate ion

THE LIFE CYCLE OF RED BLOOD CELLS

GENERAL BLOOD CELL FORMATION

Blood cell formation is called hematopoiesis or hemopoiesis. It occurs in red bone marrow. Each type of blood cell is produced in different numbers, according to the body's needs. All blood cells arise from the same type of cell called a hematopoietic stem cell or hemocytoblast.

The formation of red blood cells

This is called erythropoiesis. Red blood cells carry oxygen. If the oxygen level of the blood drops (*not the number of red cells*), the body is stimulated to produce more red blood cells, that is, more cells with an oxygen-carrying capacity. The oxygen level of the blood may drop because of:

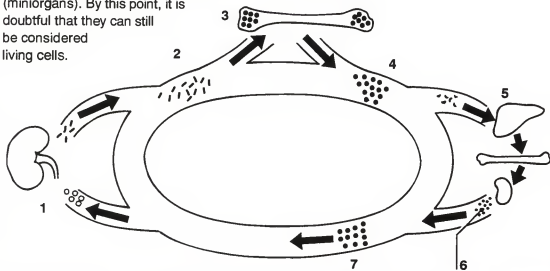
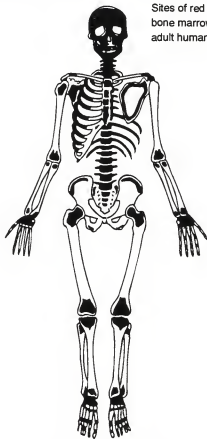
- reduced numbers of cells (caused by excessive bleeding or excess red blood cell destruction);
- reduced availability of oxygen due to high altitudes or illness (such as pneumonia); or
- increased demands for oxygen (common in people who engage in aerobic exercise).

The life cycle of a red blood cell

- 1 A low level of oxygen in the blood stimulates kidneys to produce a hormone (regulatory chemical) called erythropoietin.
- 2 The level of erythropoietin in blood rises.
- 3 This promotes the formation of red blood cells in red bone marrow.
- 4 New red blood cells are released into the bloodstream. Within a few days, they eject their nuclei (control centers) and organelles (miniorgans). By this point, it is doubtful that they can still be considered living cells.

- 5 Old and damaged red blood cells are engulfed by white blood cells living in the bone marrow, liver, and spleen. The hemoglobin (oxygen-carrying part of the cell) is broken down to be reused.
- 6 This releases the raw materials for further red blood cell formation.
- 7 New red blood cells are released into the blood.

Sites of red bone marrow in adult humans.

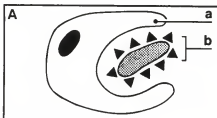


WHITE BLOOD CELLS 1: OVERVIEW OF FUNCTIONS

Leukocytes (white blood cells) are vital to the immune systems of vertebrates (animals with backbones). Once a pathogen (disease-causing substance) or foreign particle enters the body, it is largely the task of white blood cells to eliminate the threat. They can act nonspecifically (not aimed at particular substances) or specifically (aimed at particular substances).

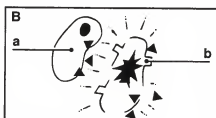
NONSPECIFIC CELLULAR IMMUNITY

Vertebrates have many nonspecific defenses, including protective bodily fluids, skin, chemical secretions, and certain types of leukocyte. Altogether, they comprise the animal's innate (inborn) immunity. Phagocytic ("engulfing") cells and cytotoxic (natural killer) cells provide cellular nonspecific defenses. Both cells attack any particle or organism they recognize as foreign.



A Phagocytes

These cells (a) engulf ("eat") pathogens (b). Neutrophils and macrophages are the main phagocytic cells.

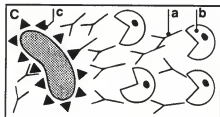


B Natural killer cells

These cells (a) are a type of lymphocyte that attacks any cancerous and foreign cells (b) and kills them.

SPECIFIC IMMUNITY

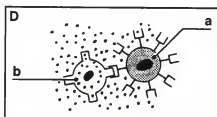
A vertebrate's specific (or adaptive) immune system is provided solely by leukocytes. Specific and nonspecific defenses involve recognition that a substance is foreign. Specific immunity also provides particular defenses for different pathogens and it "remembers" those that it has encountered before. There are two types of specific defense mechanism: humoral and cellular.



C Humoral

Humoral immunity involves the production of antibodies (proteins that attack foreign particles in the body). Specific antibodies (a) are produced by particular B-lymphocytes (or B-cells) (b) in response to different antigens (substances that provoke an immune response) (c). There are two main types of B-cells involved:

- plasma B-cells, which produce the antibodies, and
- memory B-cells, which enable the B-cells to "remember" particular antigens.



D Cellular

Cellular specific defenses are largely conducted by T-lymphocytes (or T-cells) (a). These only react to specific antigens and they can directly attack and kill harmful cells (b). There are four main types of T-cells involved:

- killer T-cells, which directly attack cells;
- helper T-cells, which act as "directors" of the whole immune response;
- suppressor T-cells, which regulate the response; and
- memory T-cells, which enable the T-cells to "remember" particular antigens.

WHITE BLOOD CELLS 2: NONSPECIFIC CELLULAR IMMUNITY

PHAGOCYTES

Phagocytes are white blood cells that engulf ("eat") pathogens (disease-causing organisms). The two main phagocytic cells are neutrophils and macrophages.

Neutrophils These are small and granular. Normally, they are the first to leave the blood and travel to the site of infection. Neutrophils die after engulfing a few foreign particles.

Macrophages These are monocytes (a type of white blood cell) that have left the blood. As well as engulfing invaders, they are responsible for clearing up dead neutrophils and other damaged cells at the site of an infection. They are larger than neutrophils. Free macrophages roam the body. Others are fixed macrophages that stay in one organ.

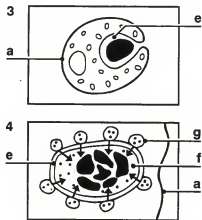
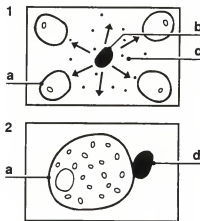
Phagocytosis

Phagocytosis is the process by which phagocytes engulf pathogens or foreign particles.

- 1 Phagocytes (a) are attracted to sites of infection (b) by chemicals (c) released during inflammation.
- 2 Once there, phagocytes must first contact and recognize the particle (d) as foreign.
- 3 The particle will then be "swallowed" by the

phagocyte. The phagocyte's cell (plasma) membrane surrounds the particle and folds inward, forming a bag (e).

- 4 This bag breaks away from the cell membrane and enters the cell. The phagocyte then digests the particle using enzymes (biological catalysts) (f) released by lysosomes (fluid-filled particles) (g).

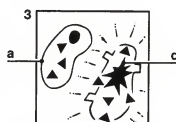
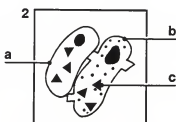
**NATURAL KILLER CELLS**

A natural killer, or cytotoxic, cell (a) is a lymphocyte (a type of white blood cell) that can kill cancerous or virus-infected cells (b).

- 1 It first recognizes an affected cell by surface changes.

- 2 The cytotoxic cell then attacks the infected cell's membrane, releasing destructive chemicals (c).

- 3 The target cell's membrane ruptures, its nucleus (d) bursts, and the cell dies.



WHITE BLOOD CELLS 3: SPECIFIC IMMUNITY (HUMORAL) (1)

Specific immunity involves two kinds of lymphocyte (a type of white blood cell): B-lymphocytes (or B-cells) and T-lymphocytes (or T-cells). These are cells that:

- can recognize and provide particular defenses for specific antigens (substances that provoke an immune response);
- use "memory" to recognize previously encountered antigens, so that an even stronger attack can be launched against them.
- The immunity provided is systemic (not limited to the site of initial infection).

The response to particular antigens is either humoral or cellular.

HUMORAL IMMUNITY

A humoral response involves the production of antibodies (proteins that attack specific antigens) by B-cells. There are many different B-cell types and each can produce a different antibody.

B-cells are assisted in this process by helper T-cells. Humoral immunity is used mainly against toxins (poisons), viruses outside body cells, and bacteria.

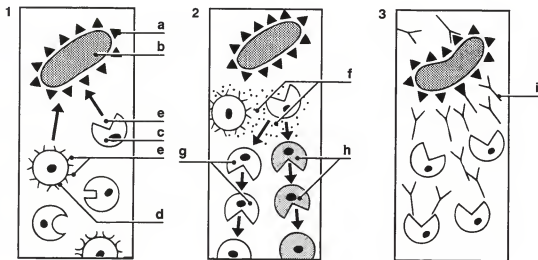
Primary response

The primary response happens on the first contact with an antigen.

- 1 The antigens (a) on a bacterium (b) are recognized by B-cells (c) and helper T-cells (d) that have the right receptors (e) for it.
- 2 The helper T-cells then secrete substances (f) that trigger the B-cells to duplicate themselves. These copies are called plasma

cells (g) and memory B-cells (h).

- 3 Plasma cells produce antibodies (i) that inactivate the antigens. These cells can produce antibodies in large numbers, at a rate of up to 20,000 per second. Plasma cells have a copious rough endoplasmic reticulum – a type of organelle (miniorgan) – that enables this.



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WHITE BLOOD CELLS 4: SPECIFIC IMMUNITY (HUMORAL) (2)

(continued from 3.54)

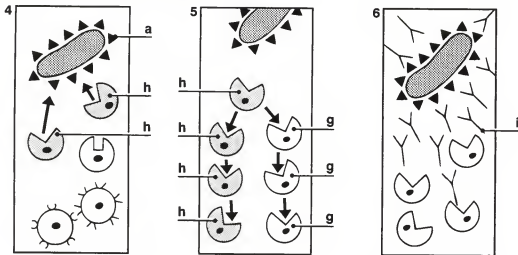
Secondary response

The secondary response happens on any subsequent contact with the same antigen. This contact may take place years after the first meeting.

- 4 If the antigen (a) enters the body again, then the memory B-cells (h) will recognize it.

- 5 They can quickly respond by producing plasma cells (g) and more memory-B cells (h).

- 6 The plasma cells will then inactivate the antigen by producing the right antibodies (i).

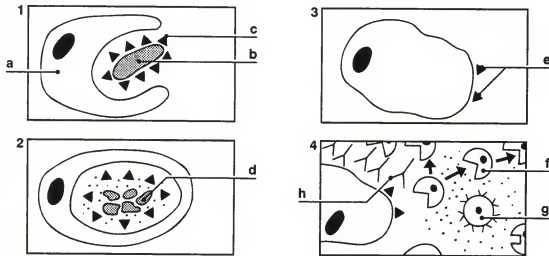
**Antigen presentation**

The process of antibody production can be helped by the activities of another type of white blood cell called a macrophage. These engulf ("eat") foreign particles.

- 1 A macrophage (a) engulfs a foreign particle (b) carrying antigens (c).
- 2 The particle is digested (d) by the macrophage. This process is called

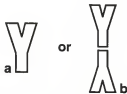




phagocytosis (cell "eating").

- 3 After processing the particle, the macrophage "displays" parts of the antigens (e) on its surface. This process is called antigen presentation.
- 4 The display acts as a signal to the B-cells (f) and helper T-cells (g) that recognize the antigen to start producing antibodies (h).



WHITE BLOOD CELLS 5: ANTIBODIES (1)

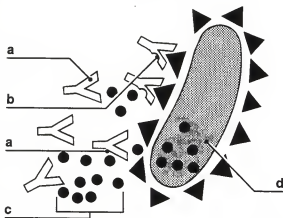
Antibodies are soluble proteins produced by a type of white blood cell called a B-lymphocyte (or B-cell). They inactivate antigens (substances that trigger an immune response). There are five main types of antibodies found in humans.

ANTIBODY STRUCTURE	LOCATIONS	FUNCTIONS
IgA 	a plasma (the watery-fluid component of blood) b saliva, tears, mucus (thick, slimy fluid), intestinal juice, and breast milk	<ul style="list-style-type: none"> Protects mucous layers and the skin from pathogens (disease-causing substances); and provides immunity to newborns in breast milk.
IgD 	attached to B-cells	<ul style="list-style-type: none"> Acts as an antigen-receptor for B-cells and helps to activate B-cells.
IgE 	skin, mucous membranes (mucus-secreting linings) of the digestive and respiratory systems, and tonsils	<ul style="list-style-type: none"> When attached to antigens, it triggers the release of chemicals that enhance inflammation.
IgG 	blood	<ul style="list-style-type: none"> Is the most common antibody; protects against viruses, bacteria, and toxins in the blood and lymph; passes from mother to fetus during pregnancy, providing some immunity for newborns; fixes complement (inactive protein circulating in the bloodstream); and is released in both primary and secondary responses.
IgM 	a attached to B-cells b free in blood	<ul style="list-style-type: none"> Acts as an antigen-receptor for B-cells; is released in the primary response; fixes complement; and is a strong agglutinating (clumping) agent.

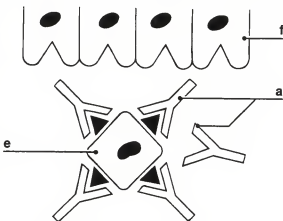
WHITE BLOOD CELLS 6: ANTIBODIES (2)

HOW ANTIBODIES WORK

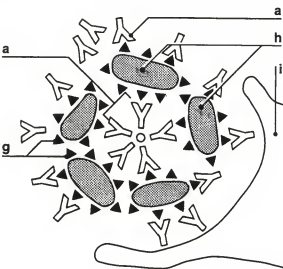
Many bacteria, viruses, and toxins carry antigens (substances that trigger an immune response). The action of antibodies on these helps to inactivate the invader in a number of ways.

**Complement fixation**

Antibodies (a) have sites (b) to which the proteins of the complement group (c) can bind. This is a group of proteins that circulates in the blood in an inactive form. Once the antibody has bound to its target cell (d), it changes shape, revealing its complement-binding site. The attached complement becomes activated and forms holes in the cell's surface. Water passes into the foreign cell, forcing it to burst. Complement also attracts phagocytic ("engulfing") cells.

**Neutralization**

Antibodies (a) can bind to certain sites on viruses (e), or toxic chemicals secreted by bacteria, to stop them from binding with tissue cells (f) of the body. The invaders will eventually be "eaten" by phagocytes.

**Agglutination**

By grouping together to bind to more than one antigen (g), antibodies (a) can develop clumps of foreign cells (h), which are more easily captured and engulfed by phagocytes (i).

WHITE BLOOD CELLS 7: SPECIFIC IMMUNITY (CELLULAR) (1)

Specific cellular immunity involves T-lymphocytes (or T-cells). These are a type of white blood cell that:

- can recognize and provide particular defenses for specific antigens (substances that provoke an immune response);
- uses "memory" to recognize previously encountered antigens, so that an even stronger attack can be launched against them; and
- differs from other white blood cells in that they can directly attack and kill infected body cells as well as foreign cells.

T-cell immune responses are directed, in particular, against viruses, cancerous body cells, and internal parasites.

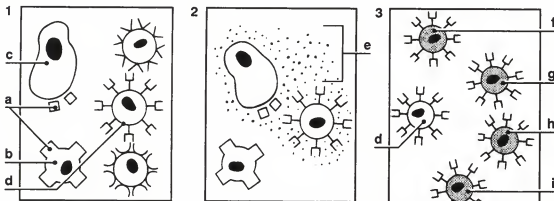
T-CELLS AT WORK

1 First, the antigens (a) on an abnormal body cell (b), or displayed in parts (called antigen presentation) by a macrophage ("engulfing" white blood cell) (c), must be recognized by T-cells (d) that are sensitized to them.

2 The macrophage and the T-cell then secrete

substances (e) that activate the T-cell.

3 The activated T-cell (d) then duplicates itself. These copies come in four subgroups: killer T-cells (f), helper T-cells (g), suppressor T-cells (h), and memory T-cells (i).



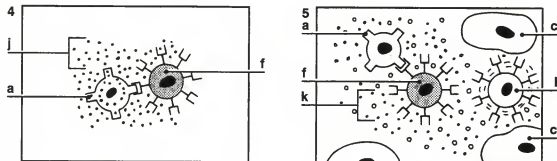
Killer T-cells

The killer T-cells (f) directly attack the infected body cells or foreign cells.

4 Once a killer T-cell has bound to an antigen (a), it releases toxic substances (j) that kill the cell.

5 It can also release substances (k) that:

- activate other white blood cells (l) in the area to become "killer" cells;
- attract macrophages (c) to the area; and
- stimulate macrophages into greater phagocytic activity.



(continued on 3.59)

WHITE BLOOD CELLS 8: SPECIFIC IMMUNITY (CELLULAR) (2)

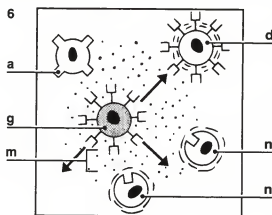
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Helper T-cells

The helper T-cells are vital to the whole immune response. They act as "directors" of the process.

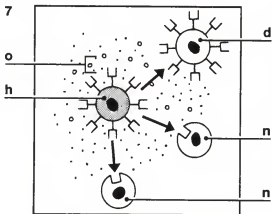
6 On recognition of the antigen (a), helper T-cells (g) secrete substances (m) that:

- stimulate the activation of both T-cells (d) and B-cells (white blood cells that produce antibodies) (n); and also
- attract other types of white blood cell to the area.

**Suppressor T-cells**

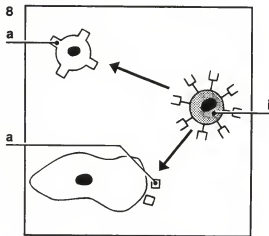
Some T-cells also have a regulatory effect on the immune response, but of a reverse nature.

7 After the threat has been eliminated, suppressor T-cells (h) release substances (o) that inhibit the activities of T-cells (d) and B-cells (n). This brings the immune response to a halt and helps prevent autoimmune ("self-inflicted") disorders.

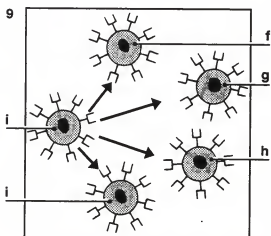
**Memory T-cells**

Some T-cells come into play on any subsequent contact with the same antigen. This secondary response may be years after the first meeting.

8 If the same antigen (a) is found in the body again, then the memory T-cells (i) will recognize it.



9 They can quickly initiate the immune response by producing the necessary T-cell duplicates: killer T-cells (f), helper T-cells (g), suppressor T-cells (h), and more memory T-cells (i).



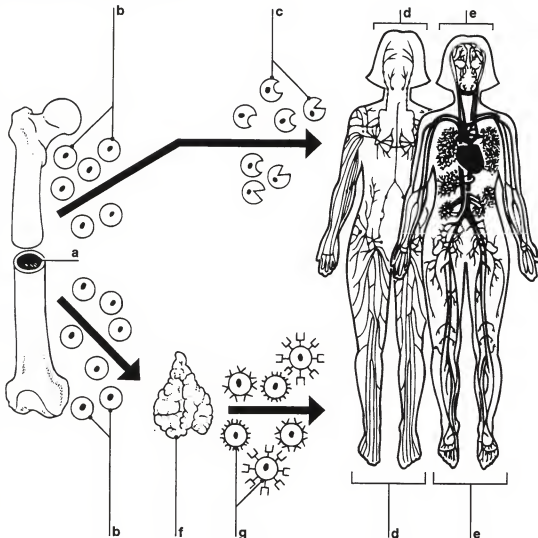
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LYMPHOCYTE DEVELOPMENT

All lymphocytes (a type of white blood cell) originate in the bone marrow (a). During fetal development, only one type of immature lymphocyte is produced by the bone marrow. A process of differentiation then occurs that turns these into either B-lymphocytes (or B-cells) or T-lymphocytes (or T-cells).

B-LYMPHOCYTES

- Those lymphocytes (b) that are to become B-cells (white blood cells that produce antibodies) probably remain in the bone marrow.
- Here, the cells duplicate and learn how to recognize one specific antigen (substance that provokes an immune response).
- The mature B-cells (c) then travel to the lymphatic (d) and blood systems (e), where they circulate until called into action.



T-LYMPHOCYTES

- Those lymphocytes (b) that are to become T-cells (white blood cells that attack and kill other cells) travel to the thymus (a gland of the lymphatic system) (f).
- Here, the cells duplicate and learn how to recognize one specific antigen.
- The mature T-cells (g) then travel to the lymphatic (d) and blood systems (e), where they circulate until called into action.

METABOLISM

The huge variety of biochemical reactions that cells carry out or take part in are collectively known as metabolism. This involves:

- anabolism (building up) of larger molecules from smaller molecules;
- catabolism (breaking down) of larger molecules into smaller molecules; and
- the creation and use of the chemical-energy storage molecule, ATP (adenosine triphosphate).

THE STAGES OF METABOLISM

NUTRITION

To fuel their metabolic processes, organisms need food.

PROTEINS

CARBOHYDRATES

LIPIDS
(FATS)H₂OCO₂**Heterotrophs**

These organisms, for example animals, need to take in ready-made foods such as plants and other animals. This food is digested (broken down) by the animal's digestive system – stomach and intestines.

Autotrophs

During photosynthesis, these organisms (such as plants) create their own foods from simple compounds (carbon dioxide and water) by using sunlight.

METABOLISM

This occurs inside cells.

AMINO ACIDS

SUGARS

GLYCEROL

FATTY ACIDS

PROTEINS

GLYCOGEN

LIPIDS

GLUCOSE

glycolysis

PYRUVIC ACID

ACETYL COENZYME A

Krebs cycle

oxidative phosphorylation

Cellular respiration

This part of metabolism largely concerns the breakdown of glucose to produce ATP.

O₂

ATP

Sites of ATP synthesis
number of ATP molecules
produced per glucose
molecule

ATP

ATP

Key:

.....> Anabolism

—> Catabolism

CO₂ Carbon dioxideH₂O WaterO₂ Oxygen

H Hydrogen

⬤ Inside a mitochondrion

O₂H₂O

ATP

The chemical-energy storage molecule ATP (adenosine triphosphate) occurs in the cells of all living organisms.

STRUCTURE

Basically, ATP is a RNA (ribonucleic acid) nucleotide (building block) with two extra phosphate groups attached.

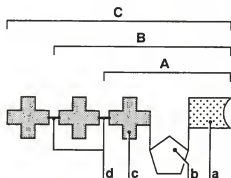
A An RNA nucleotide consisting of the

nitrogenous base adenine (a), the sugar ribose (b), and a phosphate group (c).

B If there is one extra phosphate group, the

molecule is ADP (adenosine diphosphate).

C Two extra phosphate groups joined by high-energy phosphate bonds (d) makes ATP.



FUNCTIONS

Without ATP, metabolism (all biochemical processes) ceases. ATP provides energy for:

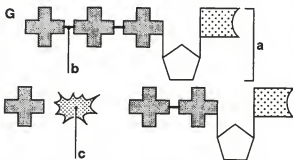
D chemical reactions that require energy;

E active (energy-using) transport across the cell (plasma) membrane; and

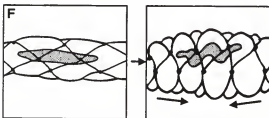
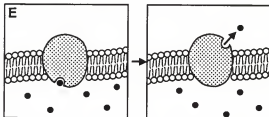
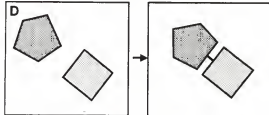
F mechanical tasks such as the contraction of muscle cells.

G Releasing energy

ATP (a) functions by releasing the energy it stores in its phosphate bonds. Breaking one bond (b) releases just enough energy (c) to fuel most biochemical tasks. The bonds are broken by hydrolysis ("splitting with water").

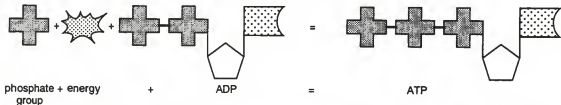


ATP



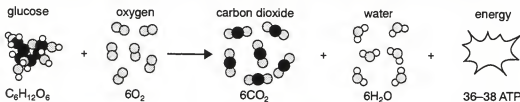
PRODUCTION

High-energy phosphate groups are transferred to ADP to turn it into ATP. This is an example of phosphorylation (the addition of phosphate). It occurs during cellular respiration, which is basically the breakdown of the sugar glucose to release enough energy to form ATP.



CELLULAR RESPIRATION 1: GLYCOLYSIS

Cellular respiration is the breakdown of the sugar glucose to release enough energy to produce the chemical-energy storage molecule ATP (adenosine triphosphate). This can be summarized by a simple equation. In reality, cellular respiration occurs in series of complex stages.



GLYCOLYSIS

The first stage is glycolysis ("sugar splitting"). It takes place in the cytoplasm (semifluid mixture) of cells. Glycolysis "invests" two ATP molecules to create four ATPs – a net gain of two ATPs.

1 Glucose activation

In a series of steps, two phosphate groups are transferred to the sugar glucose by two ATPs, which become ADP in the process. This is called phosphorylation. The end product is fructose diphosphate.

2 Sugar splitting

This sugar is split in half. The two fragments exist (reversibly) as either dihydroxyacetone phosphate or PGAL (phosphoglyceraldehyde).

3 Sugar oxidation

As PGAL, both sugars have their hydrogen removed – they are oxidized. This is done by NAD (nicotinamide adenine dinucleotide), which becomes NADH in the process. The oxidation releases energy, which is used to attach phosphate groups to the sugars.

4 ATP formation

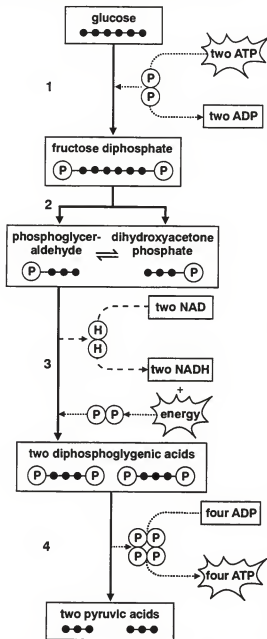
In a series of steps, the phosphate groups of the resulting acids are transferred to four ADPs. This creates four ATPs and leaves pyruvic acid – the end product of glycolysis.

If oxygen is present, the pyruvic acid enters the Krebs cycle.

If oxygen is not present, the acid takes part in anaerobic respiration (see 3.66).

Key:

- Carbon atom
- (P) Phosphate group
- (H) Hydrogen atom
- Glycolysis
- Phosphorylation
- - - Oxidation
- ⇌ Reversible states



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CELLULAR RESPIRATION 2: KREBS CYCLE

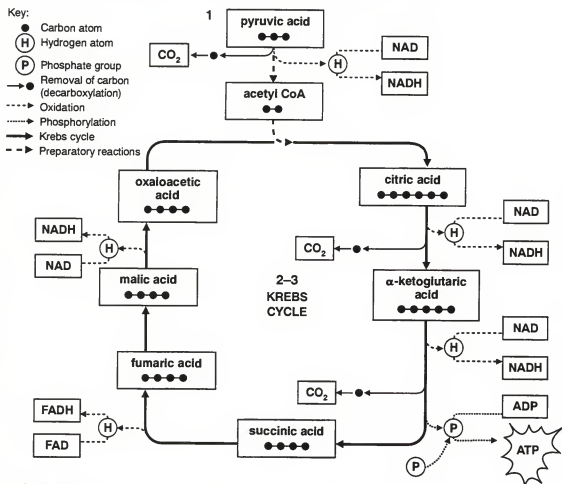
The next stage of cellular respiration is called the Krebs cycle after Hans Krebs (1900–81), who first described it in 1937. The Krebs (or citric) cycle occurs inside the mitochondria (energy-generating miniorgans) of cells.

BEFORE THE KREBS CYCLE

- 1 Pyruvic acid – the end product of glycolysis – enters the mitochondrion. It is converted into acetyl coenzyme A (acetyl CoA). This involves the removal of one carbon atom – as the gas carbon dioxide (CO_2) – and removal of hydrogen (oxidation) by NAD, which becomes NADH as a result.

THE KREBS CYCLE

- 2 Acetyl CoA, which has two carbon atoms, enters the cycle at a point where it can combine with the four-carbon compound, oxaloacetic acid. This forms the six-carbon compound citric acid.
- 3 Citric acid then undergoes a cycle of reactions in which it is reconverted to oxaloacetic acid. This acid is then available for reacting with acetyl CoA, and the cycle can continue.



End products

- The carbon dioxide removed during the cycle diffuses out of the cell and leaves the organism as a waste product. Photosynthesizing organisms might use it to create glucose using solar energy.
- One glucose molecule generates two turns of the cycle. Each turn of the cycle generates one molecule of ATP.
- At various points on the cycle, hydrogen is

removed by NAD or FAD (flavin adenine dinucleotide) and saved as NADH or FADH_2 . It is reinvested in the last stage of cellular respiration, oxidative phosphorylation.

- The Krebs cycle also provides essential materials such as the amino acids (protein building blocks) glutamic acid and aspartic acid. These are formed from α -ketoglutaric acid and oxaloacetic acid respectively.

CELLULAR RESPIRATION 3: OXIDATIVE PHOSPHORYLATION

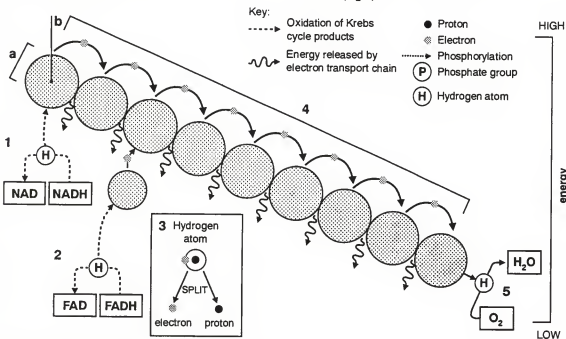
The final stage of cellular respiration is oxidative phosphorylation, in which the removal of hydrogen (oxidation) leads to the addition of phosphate groups (phosphorylation). For every glucose molecule broken down by cellular respiration, 36 or 38 molecules of ATP are generated. Either 32 or 34 of these are produced by oxidative phosphorylation.

OXIDATION AND ELECTRON TRANSPORT

Oxidation is carried out by the electron transport chain (a). This is made up of proteins (b) in the cristae (shelflike structures) inside mitochondrion.

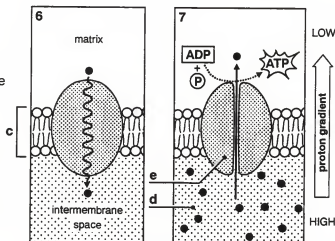
- 1 NADH produced during glycolysis or the Krebs cycle enters the chain at the "top." It is oxidized to produce NAD.
- 2 FADH produced during the Krebs cycle enters the chain slightly lower down. It too is oxidized.

- 3 The removed hydrogen atoms are split into protons (H^+) and electrons (e^-). The protons escape into the watery fluid inside the mitochondrion.
- 4 The electrons are passed down the electron transport chain. This releases energy in small, usable steps.
- 5 Ultimately, hydrogen (H) is combined with molecular oxygen (O_2) to produce water (H_2O).



PHOSPHORYLATION

- 6 The energy released by electron transport is used to pump the hydrogen protons across the inner mitochondrial membrane (c).
- 7 When a certain level is reached in the intermembrane space (d), some protons diffuse from this region of higher concentration back to the region of lower concentration in the matrix. This diffusion in the presence of the enzyme (biological catalyst) ATPase (e), provides enough energy to add a phosphate group to ADP, thus creating ATP.



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ANAEROBIC RESPIRATION

Without the presence of free oxygen, the breakdown of the sugar glucose to provide energy is called anaerobic respiration. It provides less energy per glucose molecule than aerobic respiration, which is carried out in the presence of molecular oxygen, but is at least twice as fast. Some cells can practice both types of respiration, for example:

- The skeletal muscle cells of vertebrates (animals with backbones), can function anaerobically to provide energy for extended periods of vigorous exercise.
 - Some plant root cells can function anaerobically if the soil is waterlogged.
- Anaerobic respiration produces either lactic acid or ethanol (alcohol).

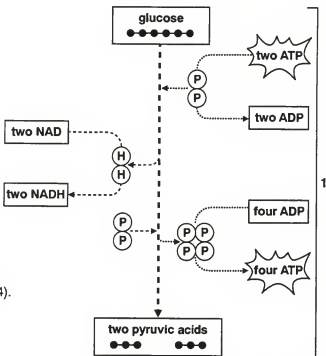
A LACTIC ACID FERMENTATION

This is carried out by animals.

- 1 Glycolysis ("sugar splitting") occurs as usual (see 3.63).
- 2 The pyruvic acids are converted to lactic acids by the addition of hydrogen. This is donated by the NADH – the reduced form of NAD (nicotinamide adenine dinucleotide) – produced during glycolysis.

End products

- Two ATPs (adenosine triphosphates); these are chemical energy storage molecules.
- Lactic acid can be reconverted into pyruvic acid by the liver and used aerobically in the Krebs cycle (see 3.64).



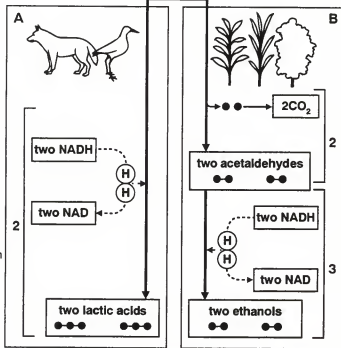
B ALCOHOLIC FERMENTATION

This is carried out by plants and yeast (a fungi).

- 1 Glycolysis occurs as usual.
- 2 The pyruvic acids are converted to acetaldehyde by the removal of carbon, which combines with oxygen to produce the gas carbon dioxide (CO_2).
- 3 The acetaldehydes are converted to ethanol by the addition of hydrogen. This is donated by NADH produced during glycolysis.

Key:

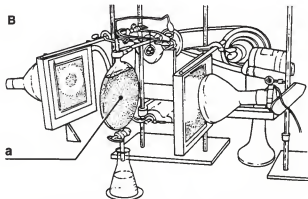
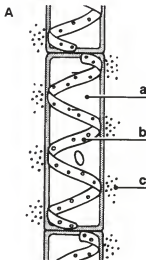
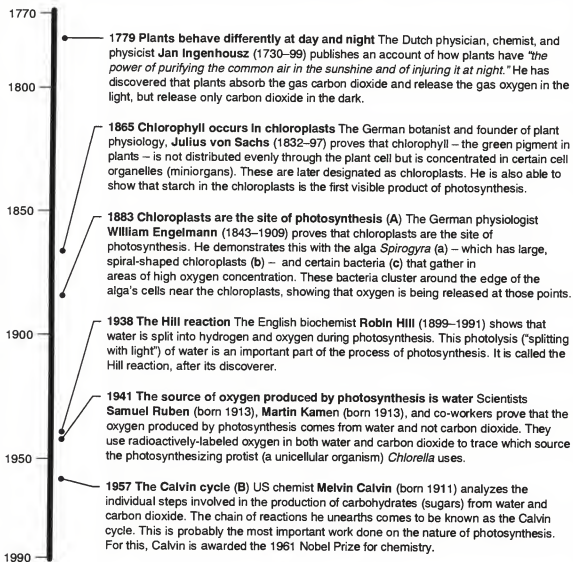
- Carbon atom
- (P) Phosphate group
- (H) Hydrogen atom
- - - Glycolysis
- - - Anaerobic respiration
- Phosphorylation (addition of phosphorus)
- > Oxidation (removal of hydrogen)
- > Decarboxylation (removal of carbon)



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THE DISCOVERY OF PHOTOSYNTHESIS

Photosynthesis is how plants – and some algae and bacteria – make food using solar energy.



Calvin's "lollipop" apparatus, which he used to trace the path taken by radioactively-labeled carbon in photosynthesis. The "lollipop" (a) was a thin, see-through vessel containing a suspension of *Chlorella*.

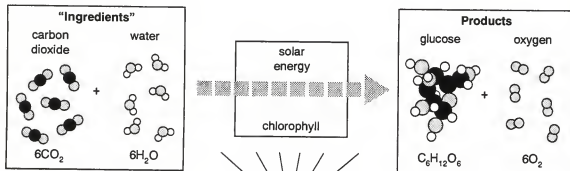
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PHOTOSYNTHESIS 1: OVERVIEW

Photosynthesis is how plants – and some algae and bacteria – make their own food. Described here is the process as carried out by plants. Bacteria perform a slightly different, simpler version of these events and some can use infrared (invisible) light.

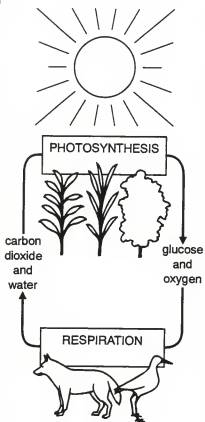
SUMMARY

- Plants use the energy of sunlight and the green pigment chlorophyll to convert the gas carbon dioxide and water into the sugar glucose. This glucose is effectively a plant's food.
- It takes six molecules each of carbon dioxide and water to produce one glucose molecule.
- A byproduct of this process is oxygen.



Sources of ingredients

- Carbon dioxide** diffuses into the plant cells from the air. It is also produced by the cell itself as a byproduct of respiration.
- Water** is taken up by osmosis (see 3.08) through the plant's roots. It is also produced by the cell itself as a byproduct of respiration.
- Light energy** is captured from sunlight by chlorophyll molecules.
- Chlorophyll** is stored inside chloroplasts. These are organelles (miniorgans) that occur in plant cells.



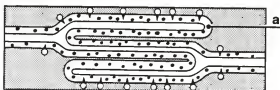
Uses of products

- Glucose** is a fuel. It is broken down during the process of cellular respiration to provide energy for cellular activities. It may be used by the cell itself, stored as starch (in plants) or glycogen (in animals), or transported to where it is needed elsewhere in the plant. Glucose is also used to make many other vital compounds that the cell needs.
- Oxygen** This escapes from the plants into the air. It can also be used in cellular respiration.

Photosynthesis is vital to life on Earth. Animals are not able to create their own food from inorganic compounds. They need to consume plants – or other animals that have consumed plants – in order to obtain products such as glucose. This, in turn, is used by cells to carry out cellular respiration (the breakdown of glucose to provide energy), which all living cells need to perform. Respiration produces carbon dioxide and water, which can be used for photosynthesis.

PHOTOSYNTHESIS 2: LIGHT REACTIONS (TEXT)

Photosynthesis occurs in a series of complex steps, not all of which need light. The light-dependent stage (or light reactions) is fueled by solar energy. It takes place in the thylakoid membranes (a) of chloroplasts.

**LIGHT HARVESTING**

- 1 Light energy enters the chloroplast.
- 2 Chlorophyll molecules (a) in the thylakoid membrane (b) channel the light energy into reaction centers (c). These centers are made up of special chlorophyll molecules. There are two types of reaction center: Photosystem I (PS I) and Photosystem II (PS II). Each has a different function.

ELECTRON TRANSFER

In this stage, the light energy absorbed by the reaction centers is used to create two different kinds of chemical-energy storage molecule: NADPH – the reduced form of NADP (nicotinamide adenine dinucleotide phosphate) – and ATP (adenosine triphosphate).

Noncyclic photophosphorylation**Production of NADPH**

- 3 Inside PS I, the light energy displaces an electron (part of an atom) from a chlorophyll molecule. This electron is transferred to an electron acceptor (d) that, in turn, donates it to a protein called ferredoxin.
- 4 Ferredoxin passes the electron to NADP, which becomes NADPH as a result.

Photolysis/Hill reaction

- 5 Also using light energy, PS II reduces water molecules (H_2O) to hydrogen (H) and oxygen (O) atoms. The oxygen is released as a byproduct of photosynthesis.
- 6 The hydrogen is stored in the thylakoid space (e). It is used to provide the hydrogen for reducing NADP to NADPH.
- 7 The hydrogen is also used in the production of ATP (steps 9–10).
- 8 This process is called the photolysis ("splitting with light") of water, or the Hill reaction after the scientist who discovered it. Photolysis releases electrons that can be donated to PS I. In this way, PS II serves to replace the electrons lost by PS I in the formation of NADPH (steps 3–4). Therefore,

PS I is able to continue donating electrons to produce NADPH, as long as PS II replenishes its supply.

Production of ATP

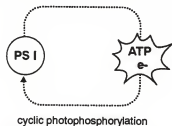
- 9 As PS II transfers electrons to PS I, hydrogen accumulates in the thylakoid membrane.
- 10 When a certain level is reached, some diffuse from this region of higher concentration to the stroma (gel-like fluid) (f) on outside of the membrane – a region of lower concentration.

This diffusion in the presence of ATPase provides the energy for the synthesis of ATP (adenosine triphosphate) from ADP (adenosine diphosphate). ATPase is an enzyme (biological catalyst) found in stalked particles (g) that dot the surface of the thylakoid membranes.

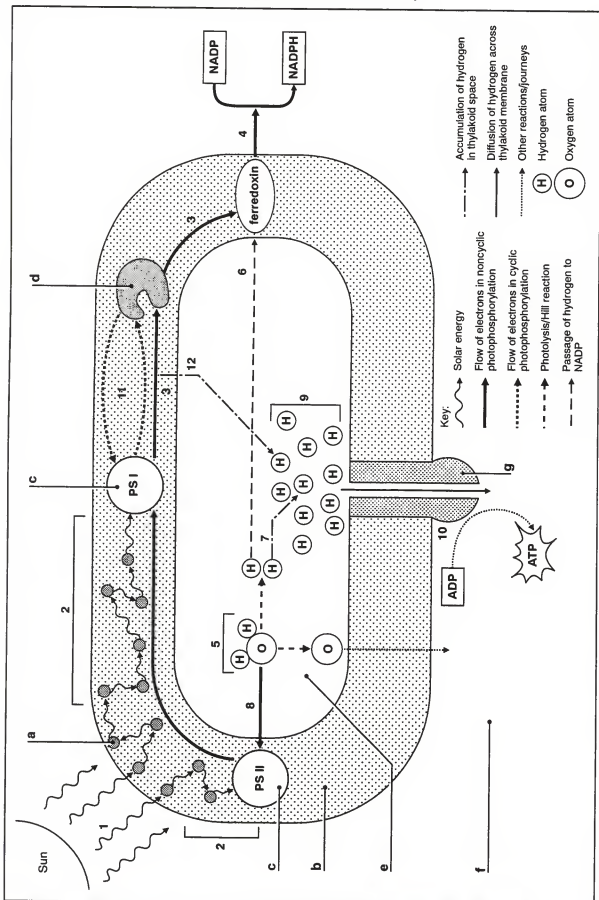
This process of ATP production by electron (e^-) transfer from PS II to PS I to NADP is called noncyclic photophosphorylation.

**Cyclic photophosphorylation**

- 11 If ATP is needed rather than NADPH, PS I passes its electrons to an electron acceptor that, in turn, returns them to PS I.
 - 12 This creates an accumulation of hydrogen ions that results in the production of ATP (as in steps 9–10).
- ATP production by electron transfer from PS I to itself is called cyclic photophosphorylation.



PHOTOSYNTHESIS 3: LIGHT REACTIONS (DIAGRAM)



PHOTOSYNTHESIS 4: DARK REACTIONS

The light-independent stage (or dark reactions) of photosynthesis is fueled by the chemical-energy storage molecules ATP and NADPH produced previously. It takes place in the stroma (gel-like fluid) (a) of chloroplasts (b).



THE CALVIN CYCLE

In the diagram, three turns of the Calvin cycle are shown at once. It takes six turns to produce one glucose molecule.

1 Each molecule of carbon dioxide (CO_2) combines with a molecule of RuDP (ribulose diphosphate). This is a sugar that contains five carbon atoms.

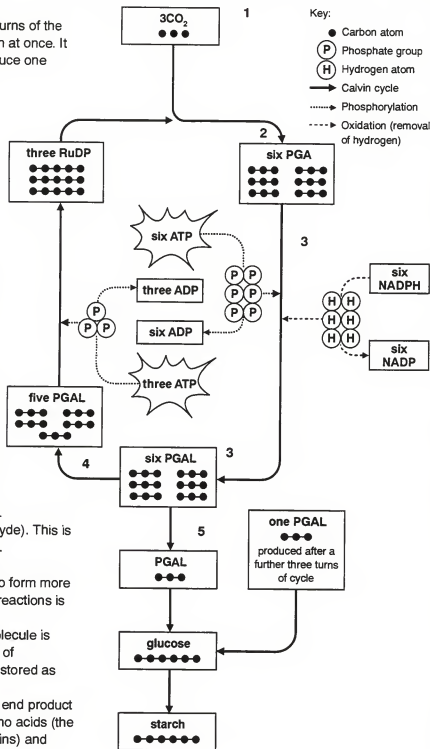
2 This forms unstable six-carbon compounds that immediately split in half to form PGA (phosphoglyceric acid). Each PGA molecule contains three carbon atoms.

3 Using NADPH and ATP, the PGAs are reduced (hydrogen is added) and phosphorylated (phosphate groups added) to form PGAL (phosphoglyceraldehyde). This is a three-carbon sugar.

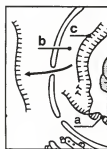
4 Five out of six PGAL molecules are used to form more RuDP. This chain of reactions is driven by ATP.

5 Every sixth PGAL molecule is used in the synthesis of glucose. This can be stored as starch molecules.

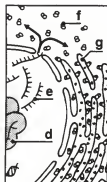
Glucose is not the only end product of photosynthesis. Amino acids (the building blocks of proteins) and lipids (fats) can also be produced.



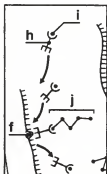
TYPICAL ANIMAL CELL AT WORK 1 (TEXT)



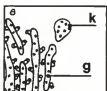
- 1 DNA (deoxyribonucleic acid) (a) in the nucleus (control center) (b) produces mRNA (messenger ribonucleic acid) (c).
- 2 mRNA passes through pores in the nuclear envelope and enters the cytoplasm (semifluid mixture) outside the nucleus.



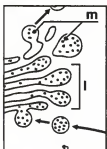
- 3 The nucleolus (a sphere of RNA and proteins) (d) in the nucleus manufactures rRNA (ribosomal RNA) (e).
- 4 rRNA leaves the nucleus and enters the cytoplasm where it is made into ribosomes (tiny, granular particles) (f). Some ribosomes become attached to the rough endoplasmic reticulum (rough ER) (g). Others remain loose in the cytoplasm.



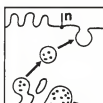
- 5 In the cytoplasm, mRNA attaches itself to ribosomes (f).
- 6 tRNAs (transfer RNAs) (h) read the protein-synthesis information carried by the mRNAs.
- 7 The amino acids (protein building blocks) (i) the tRNAs carry are bonded into polypeptide chains (j).



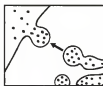
- 8 The polypeptide chains produced by ribosomes are folded up into their correct shapes inside the rough ER (g) to produce proteins (k).



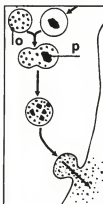
- 9 Proteins are shipped in vesicles (tiny sacs) from the rough ER to the Golgi apparatus (l).
- 10 The vesicles fuse with the wall of the Golgi apparatus.
- 11 The Golgi apparatus sorts, perhaps alters, and finally packages the proteins in Golgi vesicles (m).



- 12 Some proteins are shipped to and incorporated in the cell (plasma) membrane (n).



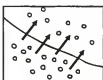
- 13 Some proteins (such as hormones and enzymes) are secreted from the cell, by exocytosis, to perform tasks elsewhere.



- 14 Some enzymes are delivered for inclusion in lysosomes (enzyme-containing sacs) (o).
- 15 Lysosomes engulf and digest harmful substances (p).
- 16 The digested particles are then expelled from the cell by exocytosis.



- 17 The cell is constantly taking in substances. Phagocytosis (cell "eating") is an example of active (energy-using) transport.

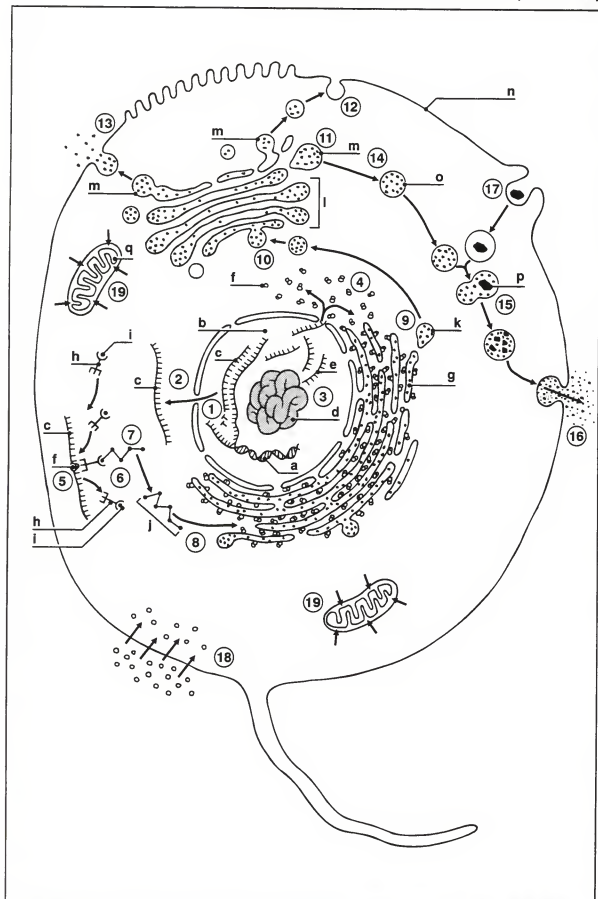


- 18 Simple diffusion across the cell membrane is an example of passive (without energy) transport.



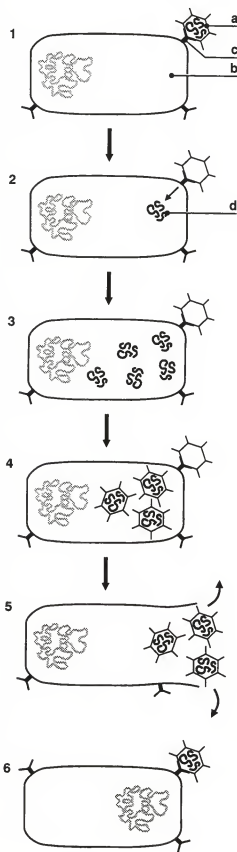
- 19 Mitochondria (q) take in fuels to produce the energy-storage molecule ATP (adenosine triphosphate), which the cell needs to carry out its activities.

TYPICAL ANIMAL CELL AT WORK 2 (DIAGRAM)



© DIAGRAM

VIRAL REPLICATION 1



The stages of viral replication vary in detail with different viruses, but the general principles are the same for all.

- 1 The virus (a) attaches to the host cell (b). This usually involves binding to a specific site (c) on the cell (plasma) membrane. Binding-site specificity explains much of what appears to be viral preferences for particular cells.
- 2 The viral genome (complete set of genes) (d) then penetrates the cell. A viral genome can be RNA (ribonucleic acid) or DNA (deoxyribonucleic acid).
- 3 The viral genome now takes over control of the cell's metabolic activities. Often this will involve shutting down the functions responsible for the cell's reproduction. The virus now uses the host's facilities and energy to replicate itself.
- 4 The viral components – genome, capsid (protein shell) and, if present, envelope – are assembled.
- 5 These new viruses are released from the cell, usually together.
- 6 Each new virus can then bind onto the membrane of a new host cell to continue the reproductive process, and hence the rate of infection of the host organism.

As they emerge, some enveloped viruses obtain part of their envelope from the nuclear (control center's) membrane or cell membrane of the host cell. This effectively disguises the virus, thus protecting it from the host organism's immune system. Herpes viruses are of this type.



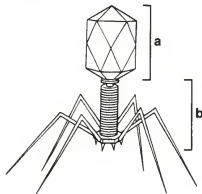
a herpes virus

VIRAL REPLICATION 2: BACTERIOPHAGES

Viruses that infect bacteria are called bacteriophages (or phages).

FEATURES

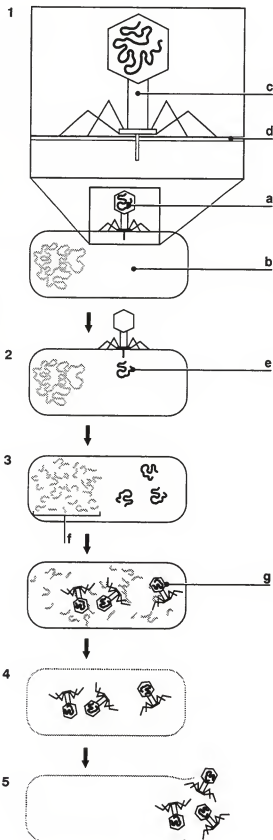
- Bacteriophages have a complex structure with a head (a) and a tail (b).
- The head contains either DNA (deoxyribonucleic acid) or RNA (ribonucleic acid).



T4 bacteriophage virus

STAGES OF BACTERIAL INFECTION

- 1 The phage (a) attaches to a bacterium (b). The tail structure (c) projects a tube that passes through the cell membrane (d).
- 2 The phage then injects its genome (complete set of genes) (e). The genome slides down the tube of the tail structure into the host.
- 3 The viral genome codes for an enzyme (biological catalyst) that breaks down the host's DNA (f). This releases nucleotides (DNA building blocks) that are then used to reassemble the viral DNA or RNA (g). The complexity of bacteriophage structure requires about 150 separate genes for its reassembly.
- 4 Toward the end of the sequences within the cell, the virus codes for the enzyme lysozyme. This breaks down the bacterial cell wall, removing the cell's protection against the effects of too much or too little water.
- 5 The cell wall ruptures and the new viruses escape.



VIRAL REPLICATION 3: HIV (1)

AIDS AND HIV

One of the most devastating immune disorders is AIDS (acquired immune deficiency syndrome). It is caused by infection with the HIV (human immunodeficiency virus).

Transmission of HIV

- HIV is present in body fluids but only blood, semen, and cervical/vaginal secretions have been proved to transmit the virus.
- The major methods of transmission are sexual contact, blood transfusions, the use of nonsterile needles, and from mother to fetus during pregnancy.

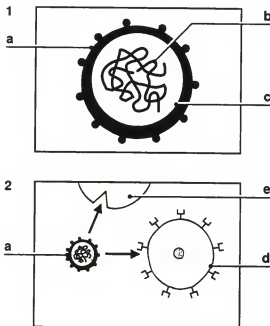
Effects of HIV infection

- In a person who is infected with HIV, the immune system is weakened.
- This can lead to the development of AIDS, in which the individual is susceptible to a variety of infections and cancers.
- In an uninfected person, these illnesses would not commonly occur or would not be serious, but they take advantage of the damage done to the immune system of an infected person. For this reason, they are called opportunistic.
- Once AIDS has developed, the condition is usually fatal.
- ARC (AIDS-related complex) may also develop in those infected with HIV. The symptoms are weight loss, fever, diarrhea, and enlarged lymph nodes.

HIV REPLICATION

- Having entered the body, the virus mainly attacks certain white blood cells.
- The most affected are the helper T-cells, which are vital for regulating the immune system.
- Macrophages ("engulfing" white blood cells), which play an important part in the body's defense against diseases, are also often affected.

- 1 HIV (a) consists of two identical strands of RNA (ribonucleic acid) (b) contained in a capsid (protein shell) (c).
- 2 HIV invades a helper T-cell (d) or another type of white blood cell (e).



(continued on 3.77)

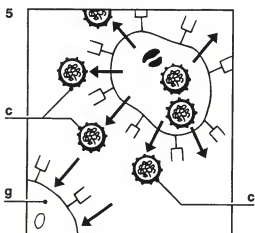
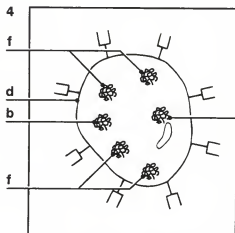
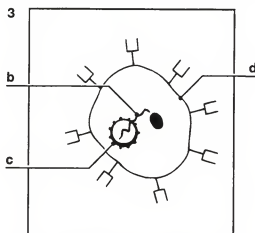
VIRAL REPLICATION 4: HIV (2)

(continued from 3.76)

3 The HIV's RNA (b) escapes from its shell (c).

4 The nucleic acid uses materials in the helper T-cell (d) to duplicate itself (f).

5 These duplicates form shells (c) and leave the host cell. This cell will then die. The new virus continues, however, to replicate using uninfected cells (g), thereby spreading the infection.

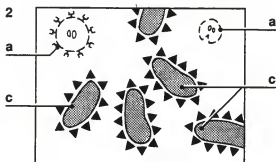
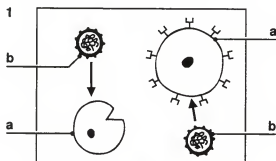


HIV AND IMMUNITY

1 In using T-cells (a) to multiply, HIV (b) destroys them.

2 As these cells (a) are vital to the working of the immune system, the virus eventually weakens the body's ability to defend itself against disease. So, pathogens (disease-causing organisms) (c) can easily invade the body and overwhelm its immune system.

Also, HIV replicates itself clumsily, making mistakes that change its protein coat. This makes it difficult for the white blood cells of the immune system to recognize new HIV viruses.



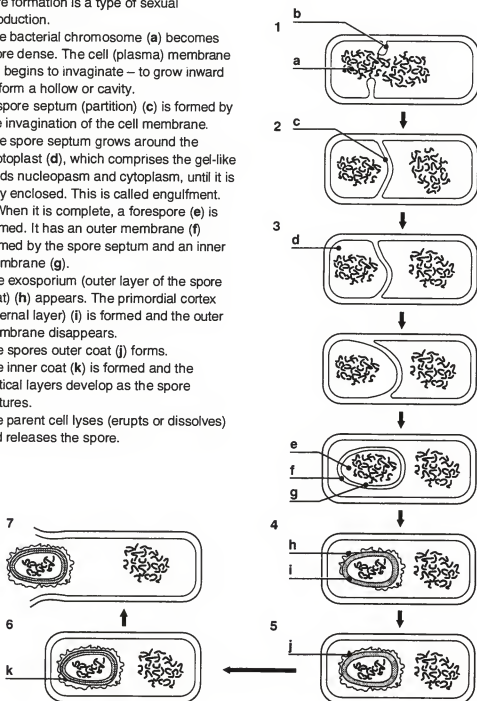
BACTERIAL SPORES

Under adverse conditions, some bacteria produce highly resistant forms known as spores. These are able to survive for long periods in conditions of high temperature, dryness, and food deprivation that would kill other organisms. When local conditions become more suitable, spores can germinate. Certain bacteria, fungi, and algae produce endospores. These are spores that form within the cell wall of the parent cell.

ENDOSPORE FORMATION

Spore formation is a type of sexual reproduction.

- 1 The bacterial chromosome (a) becomes more dense. The cell (plasma) membrane (b) begins to invaginate – to grow inward to form a hollow or cavity.
- 2 A spore septum (partition) (c) is formed by the invagination of the cell membrane.
- 3 The spore septum grows around the protoplast (d), which comprises the gel-like fluids nucleoplasm and cytoplasm, until it is fully enclosed. This is called engulfment.
- When it is complete, a forespore (e) is formed. It has an outer membrane (f) formed by the spore septum and an inner membrane (g).
- 4 The exosporium (outer layer of the spore coat) (h) appears. The primordial cortex (internal layer) (i) is formed and the outer membrane disappears.
- 5 The spore's outer coat (j) forms.
- 6 The inner coat (k) is formed and the cortical layers develop as the spore matures.
- 7 The parent cell lyses (erupts or dissolves) and releases the spore.



PROKARYOTIC CELL DIVISION

Prokaryotic organisms comprise all the varieties of bacteria. They can reproduce both asexually and sexually. Asexual reproduction as performed by prokaryotes is carried out through a process called binary fission. It is a very simple form of cell division. Sexual reproduction in prokaryotes (see 6.25) does not involve cell division or the production of new individuals.

CRITERIA FOR BACTERIAL REPRODUCTION

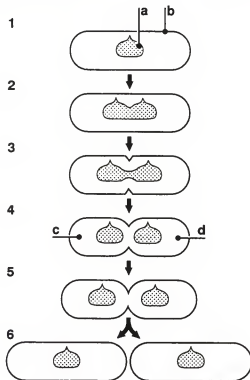
In order for bacteria to reproduce, various conditions need to be met. These include:

- adequate space;
- moisture;
- nutritional material;
- an appropriate temperature range with an optimum temperature;
- appropriate pH;
- absence of damaging radiation such as ultraviolet (UV) light;
- the presence of oxygen for aerobic bacteria;
- the absence of oxygen for anaerobic bacteria, though some can survive with or without oxygen; and
- the absence of various inhibitory substances.

BINARY FISSION

Under ideal conditions, this process may take as little as 20 minutes.

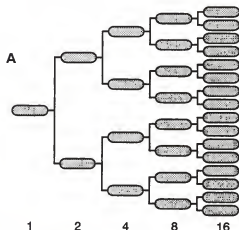
- 1 The bacterial chromosome (a) moves close to the cell membrane (b) and appears to be attached to it.
- 2 The chromosome undergoes replication so that two identical genomes (complete sets of genes) are formed.
- 3 The cell membrane pinches inward, separating the two genomes.
- 4 The septum (partition) formed by the inward pinching forces the two genomes apart so that each future daughter cell (c and d) is provided with a complete genome.
- 5 The cell becomes elongated and narrows around its equator.
- 6 The two daughter cells separate.

**Multicellular aggregations**

Not all bacteria separate into discrete individuals on reproduction. In some cases, daughter cells bud out but remain together as a multicellular aggregation.

A GEOMETRIC PROGRESSION

Theoretically, repetitive doubling of the kind produced by binary fission approaches geometric progression – doubling the population for every generation. If new individuals are moved away and adequate nutrition is provided, very large numbers will be produced in a short period of time.

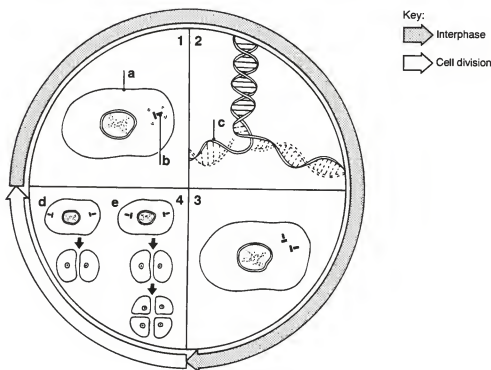


number of bacteria: 1 2 4 8 16

© DIAGRAM

LIFE CYCLE OF A EUKARYOTIC CELL

Most cells have life cycles: they are created, grow, differentiate into different cell types, reach maturity, and – when necessary – divide to reproduce. Those that do not reproduce reach maturity and then remain functional for the remainder of their life span; in the case of nerve cells this can be for as long as a hundred years. The cell cycle varies considerably from one cell type to another. The life cycle of a cell has two main periods, interphase and cell division.

**INTERPHASE**

This is the time when a cell is not dividing.

During interphase:

- the cell is metabolically active, synthesizing DNA (deoxyribonucleic acid) and proteins;
- the cell grows, increasing its dry weight; and
- the cell's chromosomes are uncondensed (uncoiled) so the chromatin in the nucleus (control center) forms a network of threads, comprising lengths of DNA wound around clumps of histone proteins.

There are three subphases of interphase during which important changes occur in preparation for cell division. The interphase timings mentioned are typical of human cells.

1 Prereplication gap (or growth₁) (G₁)

The cell (a) grows and develops and the rod-shaped centrioles (b) begin to make copies of themselves. G₁ may last for about six hours, but is greatly modified by cell type, age, and surrounding temperature. Variations in the

duration of G₁ determine the amount of time it takes for cells to increase in number.

2 Synthetic (S) phase

This subphase can last for about seven hours, during which the replication of DNA (c) occurs. This ensures that the two daughter cells formed during cell division will receive identical copies of the cell's genetic (inherited) material.

3 Premitotic gap (or growth₂) (G₂)

The second growth stage can last for about two hours. During this time further growth and development occurs, and the centrioles finish replicating so that each cell now has two pairs.

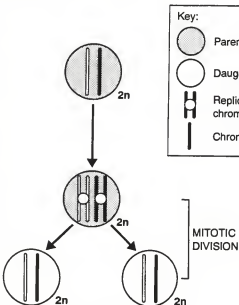
4 CELL DIVISION

In somatic (body) cells, this stage is called the M (mitotic) phase (d). Germ (reproductive) cells, which produce sex cells, undergo a different process of division called meiosis (e).

MITOSIS AND MEIOSIS: A COMPARATIVE OVERVIEW

MITOSIS

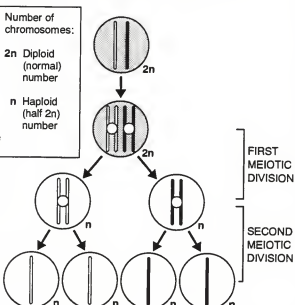
Mitosis is the process by which the somatic (body) cells of multicellular eukaryotes, such as plants and animals, reproduce themselves.



Key:
 ● Parent cell
 ○ Daughter cell
 ■ Replicated chromosome
 — Chromosome

MEIOSIS

This is the process by which germ (reproductive) cells of multicellular eukaryotes produce gametes (sex cells), such as: ova (eggs) and sperm, in animals; and pollen grains in plants.



Cells where process occurs

- In somatic cells.

- In germ cells, found in reproductive tissues.

Number of cell divisions

- One mitotic division.

- Two: the first and second meiotic divisions.

Number of resulting daughter cells

- Two cells, which are identical in every way to the parent cell.

- Four cells, which are different from the parent cell.

Chromosomes and genetic composition

- The daughter cells contain the same number of chromosomes as the parent cell.
- Each of these chromosomes is a perfect copy of the corresponding parental chromosome.

- The daughter cells have half the number of chromosomes as the parent cell.
- Meiosis can involve the crossover of genes within homologous (matching) pairs of chromosomes. The chromosomes of the daughter cells might, therefore, carry a different arrangement of genetic (inherited) information from those of the parent cell.
- The genetic composition of daughter cells is varied by the random assortment of chromosomes.

Functions

- To replace damaged cells.
- To enable growth and development.
- To ensure the genetic continuity of all body cells.

- To produce gametes.
- To ensure genetic variability of offspring (achieved by crossover and random assortment).
- To ensure that when a male and a female gamete fuse on fertilization, the resulting cell has the correct number of chromosomes (achieved by halving the number of chromosomes in the gametes, so that on fertilization the full complement of chromosomes is restored).

MITOSIS 1: PROPHASE

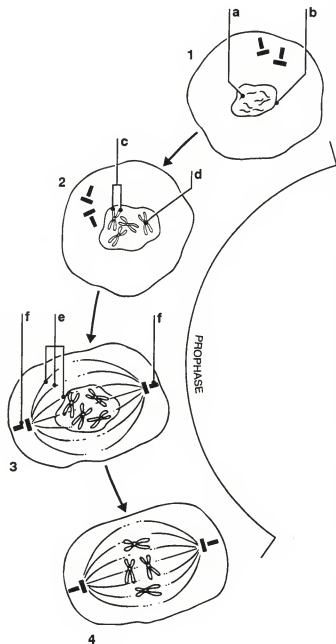
Mitosis is the process by which the somatic (body) cells of multicellular eukaryotes, such as plants and animals, reproduce themselves. During the preceding interphase stage (see 4.02) of the cell life cycle, preparations are made for cell division. These preparations include the replication of DNA (deoxyribonucleic acid) and the pair of rod-shaped centrioles.

There are four subphases of mitosis: prophase, metaphase, anaphase, and telophase. The final physical division of the cell into two parts, cytokinesis, is not strictly part of mitosis.

PROPHASE

- 1 Chromatin fibers (DNA and histone proteins) (a) disentangle from other structures in the cell's nucleus (control center) (b).
- 2 The chromatin fibers shorten and thicken, coiling up into rod-shaped chromatids (c). This allows chromosomes to become visible by light microscopy as pairs of roughly parallel sister chromatids joined near the center by a buttonlike centromere (d). Each of these X-shaped chromosomes comprises two identical chromatids formed by DNA replication during the cell's interphase.
- 3 Microtubules (tiny tubes) of the cell's cytoskeleton break down. This releases a quantity of tubulin protein, which forms the new microtubules that make the mitotic spindle (e). The two pairs of centrioles (f) separate as they are pushed apart by the fibers of the developing spindle.
- 4 The mitotic centers (the centrioles) are at the opposite ends (poles) of the cell and are joined by the fibers of the spindle. Multicellular plants do not have centrioles, but do form a spindle.

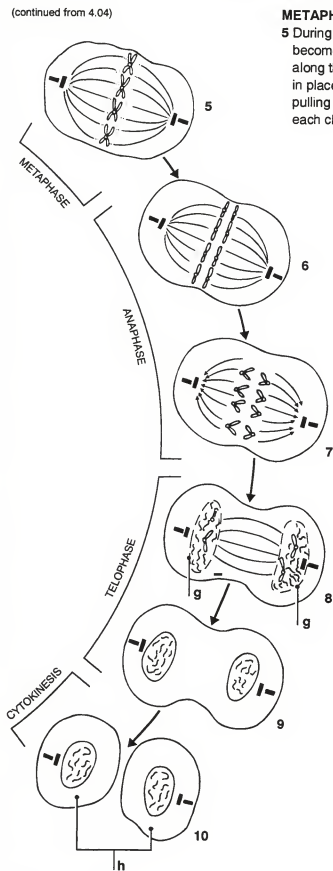
The centromere of each chromosome sprouts a brushlike tuft of microtubules on either side. These "tufts" become attached to the spindle fibers. The point of contact between a spindle fiber and a chromosome is called a kinetochore. The prophase ends with the disintegration of the nuclear envelope.



(continued on 4.05)

MITOSIS 2: METAPHASE TO CYTOKINESIS

(continued from 4.04)

**METAPHASE**

5 During metaphase, all the chromosomes become tightly coiled (condensed) and aligned along the equator of the spindle. They are held in place by the tension created by spindle fibers pulling in both directions on the centromere of each chromosome.

ANAPHASE

6 Separation of the pairs of chromatids now suddenly occurs as the centromere splits under the tension at the kinetochores. Now each chromatid becomes a chromosome in its own right.

7 Simultaneously, the cell and its spindle lengthen toward the poles. The previously-paired sister chromatids are pulled away from each other, one half of each set moves toward a different pole of the cell.

TELOPHASE

8 The chromosomes reach the poles. Each end of the elongated cell now contains an identical set of chromosomes – a complete genome. A new nuclear envelope (g) starts to form around each set of chromosomes. The chromosomes begin to unravel into chromatin as the nuclear envelopes form.

9 The cell narrows at its equator.

CYTOKINESIS

10 Cytokinesis is the physical process of cytoplasmic division or cleavage. A ring of microfilaments contracts at the cell's equator, splitting it into two daughter cells (h), which are identical to the parent cell. Strictly, cytokinesis is not part of the process of mitosis. In many species of fungi, for example, the separation into individual daughter cells does not occur, though mitosis does take place.

© DIAGRAM

MEIOSIS 1: FIRST MEIOTIC DIVISION (PROPHASE I)

Meiosis is the process by which the germ (reproductive) cells of multicellular eukaryotes, such as plants and animals, reproduce. Meiotic divisions produce gametes (sex cells). In animals, the gametes ova (eggs) and sperm are derived from meiosis in the female and the male respectively. In plants, pollen grains are the gametes. Meiosis produces sex cells with half the parental number of chromosomes. This ensures that when a male and female sex cell fuse on fertilization, the resulting fertilized cell has the correct number of chromosomes – half from each parent – and no more. There are two meiotic divisions and this halving occurs during the first meiotic division, which is sometimes referred to as the “reduction division of meiosis.”

During the preceding interphase stage of the cell life cycle, preparations are made for meiosis. These include the replication of DNA (deoxyribonucleic acid) and the pair of centrioles.

PROPHASE I

- 1 Chromatin fibers (DNA and proteins) (a) disentangle from other structures in the nucleus (control center) (b).

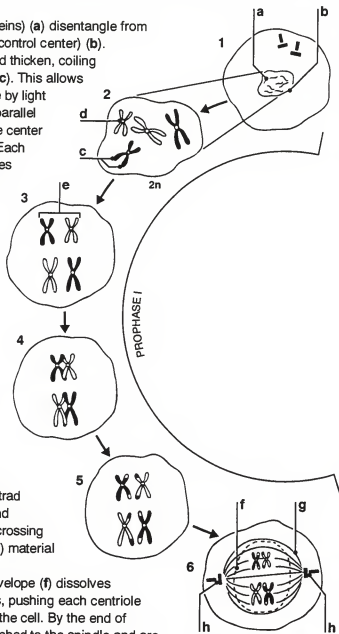
- 2 The chromatin fibers shorten and thicken, coiling up into rod-shaped chromatids (c).

This allows chromosomes to become visible by light microscopy as pairs of roughly parallel sister chromatids joined near the center by a buttonlike centromere (d). Each X-shaped chromosome comprises two identical chromatids formed by DNA replication during the cell's interphase.

- 3 Synapsis occurs: homologous (matching) chromosomes pair up and become linked closely together to form structures called tetrads (e). An exact pairing of corresponding points along their lengths occurs as they lie side by side. The chromosomes that comprise homologous pairs are derived one from the mother (the maternal chromosome) and one from the father (the paternal chromosome).

- 4–5 An event called crossover might occur: chromatids within each tetrad break at corresponding points and exchange lengths of DNA. This crossing over mixes the genetic (inherited) material derived from the two parents.

- 6 Meanwhile, the cell's nuclear envelope (f) dissolves and the meiotic spindle (g) forms, pushing each centriole pair (h) toward opposite ends of the cell. By the end of prophase I, the tetrads have attached to the spindle and are moving toward the cell's equator.



Number of chromosomes:
 2n Diploid number
 n Haploid number

(continued on 4.07)

© DIAGRAM

MEIOSIS 2: FIRST MEIOTIC DIVISION (METAPHASE I TO CYTOKINESIS)(continued from 4.06) **METAPHASE I**

7 The tetrads align themselves along the spindle's equator during metaphase I. The alignment is random, so either the maternal or paternal chromosome of a homologous pair can be on a given side of the equator.

ANAPHASE I

8 The tetrads separate and the constituent chromosomes of each move to opposite ends (poles) of the cell. (The sister chromatids still remain together, it is just the tetrads that break up.)

As the alignment during metaphase I was random, maternal chromosomes will move arbitrarily to either pole of the cell. The same applies to the paternal chromosomes. This random assortment provides yet another mechanism for genetic mixing. In combination with crossover, it ensures genetic variability – the reason that offspring differ in many characteristics from their parents.

TELOPHASE I

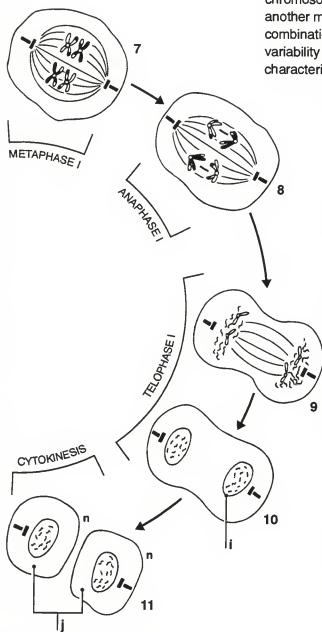
9 The chromosomes begin to unravel.
10 Nuclear envelopes (l) form around the chromatin masses at each pole, and the spindle disappears.

CYTOKINESIS

11 A ring of microfilaments (tiny fibers) contracts at the cell's equator, splitting it into two daughter cells (j).

RESULTS OF FIRST MEIOTIC DIVISION

- Each daughter cell has half the number of chromosomes (the still-united sister chromatids are considered to be one chromosome) as the parent cell – the n or haploid chromosome number.
- Each daughter cell still has the same amount of genetic information as the parent cell – the diploid amount of DNA – thanks to DNA replication prior to meiosis. This amount comprises two copies (the sister chromatids) of only half of the original material, however.
- The chromosomes of the daughter cells also carry a different arrangement of genetic information from those of the parent cell – thanks to crossover and random (or independent) assortment.



MEIOSIS 3: SECOND MEIOTIC DIVISION

After the completion of the first meiotic division, the resulting two daughter cells enter a period called interkinesis before the second meiotic division begins. Interkinesis is similar to the interphase of the cell life cycle. Preparations are made for the second division: the centrioles are replicated but DNA replication does not occur.

The second meiotic division is similar to mitosis, except that as no prior DNA replication has occurred the chromosomes are simply shared equally between the resulting four daughter cells. For this reason, this second division is sometimes called the "equational division of meiosis."

PROPHASE II

- 1 The nuclear envelopes (a) break down.
- 2 The meiotic spindles (b) re-form with each X-shaped chromosome (c) attached to each of the centriole pairs (d) by spindle fibers.

METAPHASE II

- 3 The chromosomes line up along the equators of the spindles.

ANAPHASE II

- 4 The chromatids that form each chromosome are pulled apart, exactly as in mitosis. They are pulled toward opposite ends of the cells from each other. Now each chromatid becomes a chromosome in its own right.

TELOPHASE II

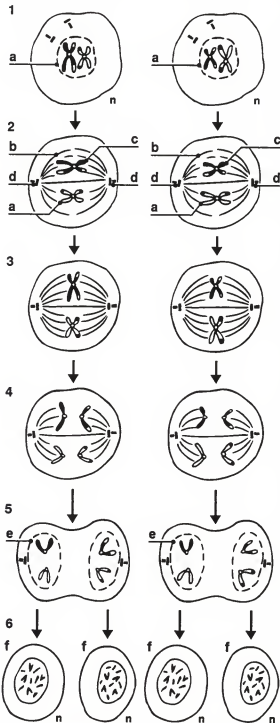
- 5 Nuclear envelopes (e) start to re-form around each set of chromosomes; the chromosomes begin to unravel; the spindles disappear; and the cells narrow at their equators.

CYTOKINESIS

- 6 A ring of microfilaments contracts at the cells' equators, splitting each cell into two daughter cells (f).

RESULTS OF SECOND MEIOTIC DIVISION

- Each of the four daughter cells still carries the haploid (n) number of chromosomes (half that of the original parent cell) – after the X-shaped chromosome is split up during anaphase II, each chromatid is considered to be one whole chromosome.
- Each of the daughter cells now also carries the haploid amount of DNA, as the sister chromatids have been equally shared between the four daughter cells.



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HOMOLOGOUS CHROMOSOMES AND CROSSOVER

HOMOLOGOUS CHROMOSOMES

In the cells of eukaryotes, such as plants and animals, all the chromosomes fall into homologous (matching) pairs except for those in the gametes (sex cells). Each pair comprises one chromosome (or homologue) from the mother and one from the father. Both the maternal and the paternal homologue of a pair carry – in the same order along the chromosome – the genes that code for the same traits, but not necessarily for the same expression of these traits. The maternal homologue may code for blue eyes and the paternal one for brown eyes, for example.

Although the sex chromosomes X and Y do not match physically, they behave as a homologous pair during cell division.

Homologues and cell division

During normal cell division (mitosis), the new cells receive a copy of each homologue. During meiosis (the cell division that produces gametes), however, the cells only receive one member each of a homologous pair. This homologue might carry genes from both the maternal and paternal chromosome of the original pair. This is achieved by crossover.

CROSSOVER

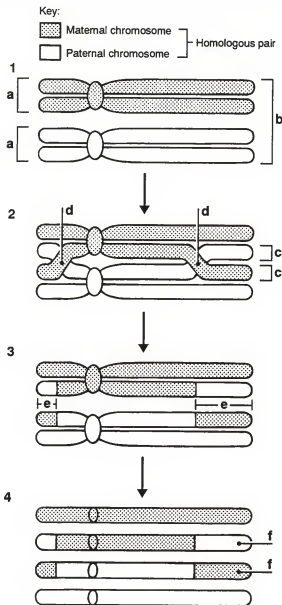
Crossover happens during prophase I of meiosis. It can occur anywhere along the length of the homologues and appears to be a random process. It mixes the genetic material – the DNA (deoxyribonucleic acid) – inherited from both parents, so that new combinations of genes are formed.

During prophase I

- 1 Synapsis occurs: homologous chromosomes (a) pair up and become linked closely together to form structures called tetrads (b). An exact pairing of corresponding points along their lengths occurs as they lie side by side.
- 2 Chromatids (c) within the same tetrad, but on different chromosomes, become wrapped around each other forming chiasmata (points of contact) (d).
- 3 The chromatids break and rejoin at these chiasmata to exchange corresponding lengths of DNA (e).

After meiosis

- 4 The tetrads and the chromosomes have broken up into their constituent chromatids – each of which is now a chromosome in its own right. Two of the resulting chromosomes are called recombinant chromosomes (f) as they carry new combinations of genes derived from both parents.



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GAMETE FORMATION IN HUMANS 1: OOGENESIS

Oogenesis is the formation of a female gamete, an ovum (egg). It starts before birth and, unlike the production of sperm (male gametes), becomes a cyclical process by puberty. Each cycle (steps 3–5) lasts about 28 days and is repeated throughout a woman's reproductive years.

location of the ovaries



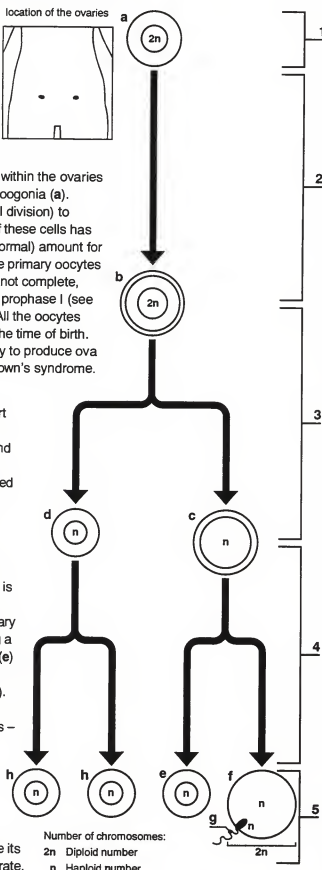
BEFORE BIRTH

- 1 During fetal development, certain cells within the ovaries change to become what are known as oogonia (a).
- 2 Oogonia divide by mitosis (ordinary cell division) to make thousands of other cells. Each of these cells has 46 chromosomes – the $2n$ or diploid (normal) amount for humans. The cells enlarge and become primary oocytes (b). The primary oocytes begin, but do not complete, meiosis (sex cell division). They halt at prophase I (see 4.06) until puberty, 10–14 years later. All the oocytes that a woman will have are present at the time of birth. This is why older women are more likely to produce ova with mutations, such as that causing Down's syndrome.

FROM PUBERTY

- 3 Each month, some primary oocytes start to grow, and one dominates. The dominating oocyte continues meiosis and produces one cell called a secondary oocyte (c) and another, smaller cell called the first polar body (d). Both cells have only 23 chromosomes each – the n or haploid (half $2n$) amount.
- 4 The secondary oocyte begins to divide, but it is at this point that ovulation (the process by which the secondary oocyte is released from the ovary) occurs.
- 5 If fertilization takes place, the secondary oocyte completes its division, producing a small cell called the second polar body (e) and another, larger cell called the ovum (f). The ovum is fertilized by a sperm (g). The resulting zygote (fertilized egg) has the diploid ($2n$) amount of chromosomes – 23 from the ovum and 23 from the sperm. The first polar body may divide to produce two even smaller polar bodies (h). All the polar bodies will then degenerate.

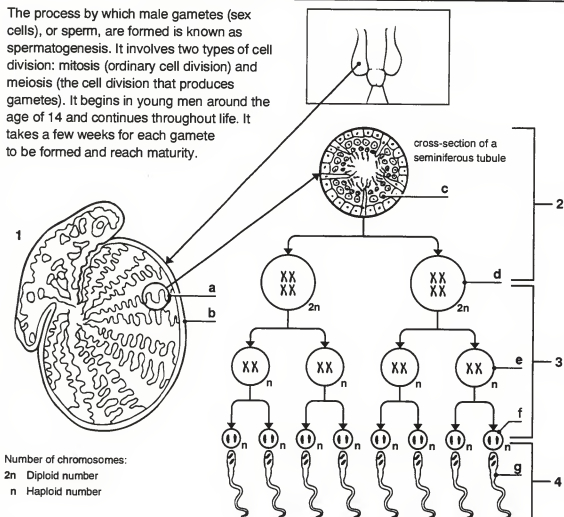
If fertilization does not take place, the secondary oocyte does not complete its meiotic division and all the cells degenerate.



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GAMETE FORMATION IN HUMANS 2: SPERMATOGENESIS

The process by which male gametes (sex cells), or sperm, are formed is known as spermatogenesis. It involves two types of cell division: mitosis (ordinary cell division) and meiosis (the cell division that produces gametes). It begins in young men around the age of 14 and continues throughout life. It takes a few weeks for each gamete to be formed and reach maturity.

**1 INSIDE THE TESTES**

Spermatogenesis takes place within seminiferous tubules (coiled tubes) (a) inside the testes (b). The seminiferous tubules are lined with immature cells called spermatogonia, or stem cells (c). Each stem cell has 46 chromosomes – the 2n or diploid (normal) amount in humans.

2 Mitosis

Spermatogonia multiply by mitosis, and the cells that are produced are called primary spermatocytes (d). These carry the same number of chromosomes as their parent cells – they still have 46 each.

3 Meiosis

First meiotic division The primary spermatocytes then divide by meiosis to produce secondary spermatocytes (e). These

cells have 23 chromosomes each – the n or haploid (half 2n) number of chromosomes.

Second meiotic division The secondary spermatocytes divide to produce spermatids (f), still with 23 chromosomes in each cell.

4 SPERMIOGENESIS

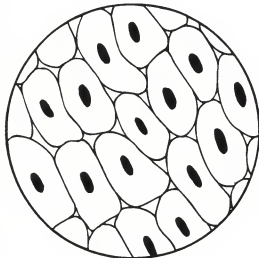
The final stage of spermatogenesis is called spermiogenesis. It occurs when spermatids mature into spermatozoa (or sperm) (g). This maturation takes place as the spermatids are forced up the vasa deferentia (narrow tubes that carry sperm from the testes to the penis).

FERTILIZATION (not shown)

When the sperm fuses with a female gamete (an ovum, or egg), the resulting zygote (fertilized egg) has the diploid (2n) amount of chromosomes – 23 from the father's sperm and 23 from the mother's ovum.

CANCER 1: FEATURES OF CANCER CELLS

When cell division goes wrong, cancer can develop. Cancer is a form of abnormal cell growth. It is more harmful than other forms such as warts. This is because a cancerous growth is malignant and not benign (localized and relatively harmless). Malignant growths are able to metastasize (spread around the body through blood and lymph vessels) and invade surrounding tissues, causing damage.



normal cells



cancerous cells

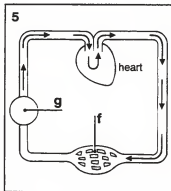
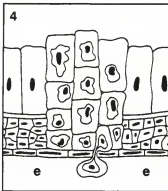
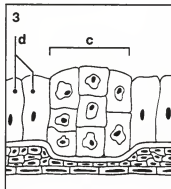
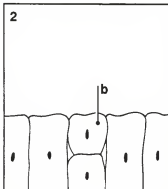
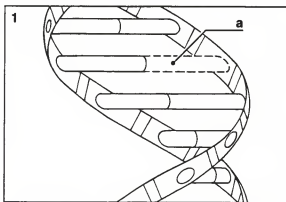
FEATURES OF CANCER CELLS

- Marked chromosomal abnormalities.
- They are more spherical than normal cells.
- Cancerous cells have relatively large nuclei (control centers).
- They often have coarsely-clumped chromatin fibers – DNA (deoxyribonucleic acid) and histone proteins.
- They form uncontrolled masses as they have lost the normal controls on growth. They have become "immortal."
- Having become independent of the factors normally needed for cell growth, they are said to be "transformed."
- Cancerous cells do not divide more rapidly than normal cells. The S phase (see 4.02) for several solid cancers lasts roughly 20 hours; and for several leukemias it takes about 60 hours. These are longer times than for normal cells.
- Cancerous cells usually reflect the features of the tissue from which they derive. The

- less cancer cells retain these features, the more dangerous they are. Well-differentiated cancer cells are usually less aggressive and dangerous than immature-looking, poorly-differentiated cells. Undifferentiated cells are said to be anaplastic or highly malignant. Anaplastic cells have reverted to a simpler form and are generally smaller than the cell type from which they derive, but can sometimes be larger.
- Cancerous cells have the ability to penetrate normal tissue barriers, allowing invasion of lymphatic or blood vessels, so they are able to spread to remote parts of the body.
- They cannot adhere well to surfaces.
- Cancerous cells can grow without being anchored to a surface.
- They can set up new colonies in the body called metastases.
- They can start up cancers in other individuals if introduced into their bodies.

CANCER 2: DEVELOPMENT, SPREAD, AND CAUSES**DEVELOPMENT AND SPREAD**

- 1 Cancerous cells arise from a single cell with abnormal DNA (deoxyribonucleic acid). Its DNA has undergone a mutation (a) in the sequence of genes that promote cell growth. These mutated genes are called oncogenes.
- 2 The altered cell (b) reproduces through division. Usually, mere contact between adjacent cells may help limit the amount of cell division occurring in tissues. Cancerous cells have lost this contact inhibition, however, and divide in an uncontrolled manner.
- 3 The multiplying cancer cells form a primary tumor (c) if left unchecked. Cells from this tumor invade surrounding tissues, causing damage to healthy cells (d).
- 4 Eventually, cancerous cells can break into a nearby blood or lymph vessel (e).
- 5 They are then able to metastasize (travel around the body) and develop secondary cancerous sites (metastases) in tissues (f) a long way from the primary site (g). Less than one in a thousand cells entering the bloodstream will do this though.

**CAUSES****Carcinogens**

Certain agents, called carcinogens, play a role in causing cancer. They include:

- ionizing radiation (X rays in high doses, for example);
- ultraviolet (UV) rays in sunlight;
- a wide range of chemical poisons (those in tobacco, for example);
- asbestos fibers; and
- certain fungi.

Viruses

- Oncoviruses introduce foreign DNA into genomes (complete sets of genes).
- Certain viruses have been linked with otherwise rare forms of cancer – HIV (human immunodeficiency virus) and Kaposi's sarcoma, for example.

Other factors

- Cancer development also depends on various

environmental factors such as diet, alcohol intake, and stress.

- In general, the incidence of cancer rises with age, but it is not known exactly why.
- The tumor-suppressor genes present in normal cells may be turned off by mutations or may be defective as a result of an inherited mutation. This can result in a hereditary predisposition to cancer.



BASIC CONCEPTS 1: GENES AND CHROMOSOMES

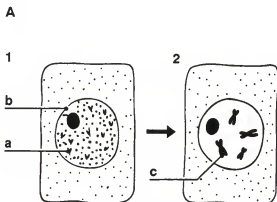
Genetics is the study of the inheritance – why do the offspring of organisms always resemble their parents, so that dogs never give birth to cats, and why do offspring tend to resemble their parents more than other members of their species? Classical genetics (covered from 5.03 on) is largely concerned with how early investigators unraveled basic concepts such as those described here. Many of the techniques they devised in the process are still used today.

GENES AND CHROMOSOMES

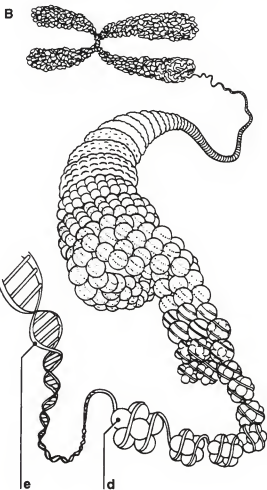
Inherited factors that determine the characteristics of an individual are called genes. They are found in chromosomes. In eukaryotes (such as plants and animals), chromosomes occur in the nucleus (control center) of each cell. In prokaryotes (bacteria), the chromosome is free inside the cell. Classical genetics is largely concerned with eukaryotic genes.

A Appearance of genetic material

- 1 For most of a eukaryotic cell's life, the chromosomes are not visible but are dispersed as chromatin fibers (a) inside the nucleus (b).
- 2 When a cell is about to divide, the chromatin fibers condense and the X-shaped chromosomes (c) become visible under a microscope.

**B Structure of a chromosome**

A chromosome is constructed of proteins (d) and DNA (deoxyribonucleic acid) (e). Each chromosome carries several hundred or several thousand genes.

**Function of genes**

Genes provide the design, or "blueprint," for an individual. In humans, for example, they determine eye color, height, and hair color. Tiny differences in genetic information make each organism unique.

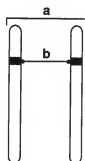
HOW GENES WORK

- A gene provides each cell in the body with instructions for making a particular protein (or part of a protein). Protein synthesis is described in section six.
- Each protein, either directly or indirectly, determines a particular characteristic. Proteins can be enzymes (biological catalysts) or structural proteins, which form part of the cell or tissue structure.

BASIC CONCEPTS 2: ALLELES, GENOTYPE, AND PHENOTYPE

ALLELES

In most eukaryotes, genes for a particular feature occur in pairs: one gene on each chromosome of a homologous (matching) pair (a). These paired genes are called alleles (b).



Homozygous alleles

When alleles are identical (they have the same DNA sequence), the individual is said to be homozygous for that gene. For example, both alleles might be for brown eyes (*B*).

Heterozygous alleles

If the paired genes consist of different alleles, the individual is said to be heterozygous. For example, one allele might be for brown eyes (*B*) and the other for blue eyes (*b*).

Dominant and recessive alleles




One allele may be dominant: its characteristic (for example, brown eye color) is expressed in preference to the characteristic of the other allele (for example, blue eye color). The "weaker" allele is called recessive.

GENOTYPE

Genotype refers to the genetic constitution of an individual. It indicates the combination of alleles. For example, a homozygous brown-eyed individual has the genotype *BB* – both alleles are for brown eye color.

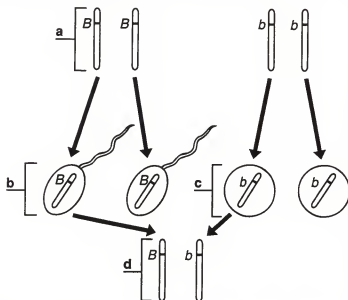
PHENOTYPE

Phenotype refers to the individual's observable characteristics resulting from his or her genotype. For example, an individual with the *Bb* genotype has the brown eye-color phenotype – so he or she has brown eyes.

	HOMOZYGOUS		HETEROZYGOUS
Alleles	<i>B</i>  <i>B</i>	<i>b</i>  <i>b</i>	<i>B</i>  <i>b</i>
Genotype	<i>BB</i>	<i>bb</i>	<i>Bb</i>
Phenotype	brown eyes	blue eyes	brown eyes

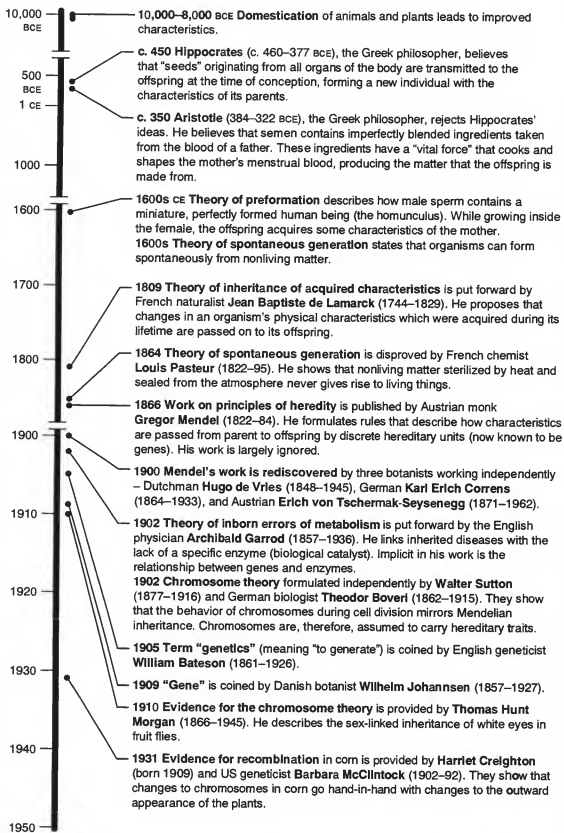
Inheriting a genotype

Genes from the parents (a) are carried in gametes (sex cells). In plants, a gamete is usually a pollen grain or spore. In animals, these gametes are the female ova (eggs) and the male sperm. Each male gamete – in this case, sperm (b) – contains one set of chromosomes which combines with the set in the ovum (c) to form the genotype of the new individual (d). Which male gamete fertilizes a particular female gamete is regarded as a random event.



THE STUDY OF INHERITANCE THROUGH THE AGES

This timeline shows some of the main landmarks in the study of inheritance leading up to the middle of the twentieth century.



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STUDYING INHERITANCE EXPERIMENTALLY

To study how characteristics are inherited by offspring from their parents, an organism must be chosen to use in breeding experiments. There are several factors that influenced the choice of organisms made by the early pioneers of genetics.

MAINTENANCE OF ORGANISM

The organism must be easy to handle and maintain. A herd of cattle would be much harder to keep and feed, for example, than a jar full of fruit flies.

VARIATION

There must be some readily distinguishable natural varieties to test, such as flower color or stem length. It is also important that these varieties show discrete characteristics. If breeding purple-flowered plants with white-flowered plants, for example, it is not useful if the offspring have every possible shade of color between purple and white.

Hypothetical example of an experimental organism:

Species: *X flower*

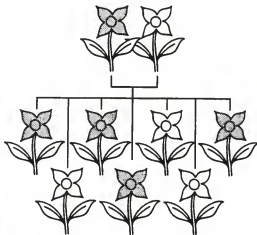
All possible variations of petal color in *X flower*:

a *X flower* with white flowers

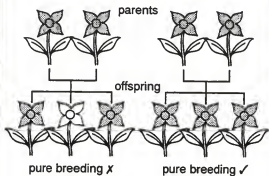
b *X flower* with purple flowers

**NUMBERS OF OFFSPRING**

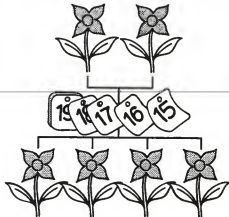
Large numbers of offspring must be produced from each mating to enable the experimenter to interpret the results correctly. By analogy, if you wanted to test whether there is an equal probability that a tossed coin lands either heads or tails up, you would have to toss it a large number of times to show that there is not even a slight preference in the way it lands.

**PURE-BREEDING STRAINS**

The background of the first individuals used in the experiments must be known, so that only pure-breeding (pedigree) individuals are used. It would not be useful to cross a purple-flowered plant with a white-flowered plant if the purple-flowered plants, when crossed with each other, produced offspring that did not all have purple flowers.

**LIFE CYCLE**

The organism must have a short life cycle. This ensures that the offspring from one mating quickly reach maturity, so that they too can be used in breeding experiments.



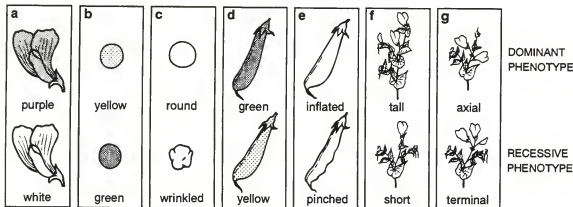
More recently, knowledge of genetics has grown to the state where it is possible and useful to use organisms that do not conform to all of these criteria.

GREGOR MENDEL 1: THEORY OF PARTICULATE INHERITANCE

Gregor Mendel (1822–1884) was an Austrian monk who carried out breeding experiments with the garden pea (*Pisum sativum*). He crossed varieties of peas that had seven, clearly-distinguishable physical traits:

- a flower color; d pod color; g flower
b seed color; e pod shape; placement.
c seed shape; f stem height; and

The physical appearance of each of these traits is called an organism's phenotype – though Mendel used the term "character." A plant could have the phenotype of purple flowers, for example, or white flowers.



THEORY OF PARTICULATE INHERITANCE

Mendel manually pollinated his pea plants so that he could either cross two individuals or cause one plant to mate with itself (self-pollination). At first, he only studied one particular trait at a time.

1 Parental (P) generation

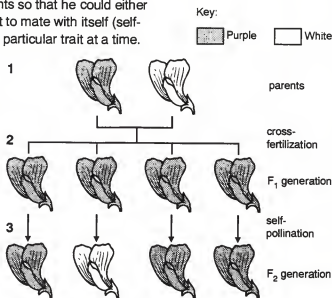
In this example, a pure-breeding, purple-flowered plant was crossed with a pure-breeding, white-flowered one.

2 First (F_1) generation

The offspring were all purple flowered.

3 Second (F_2) generation

When these offspring were then self-pollinated, the resulting plants could have either white or purple flowers.



Mendel's conclusions

After many experiments, Mendel proposed that a plant's phenotype for each trait is determined by two "particles" or "factors" (hereditary units) – one from each parent.

- In this example, the factor took two forms: one for purple and another for white flowers.
- Mendel reasoned that the factor for white flowers had been carried from the parental white flowers, through the F_1 generation, and into the F_2 generation.

- The F_1 generation therefore contained factors for both purple and white flowers.
- Mendel used the term "dominance" to describe how the purple-flower factor masked the white-flower factor.
- The white-flower factor was said to be "recessive" to the purple factor.

These "factors" are now known to be genes. The different forms a gene can take (purple or white flowers, for example) are called alleles.

GREGOR MENDEL 2: PRINCIPLE OF SEGREGATION

Mendel proposed that the two forms (alleles) of a gene separate (segregate) from each other in the formation of gametes (sex cells). This is called the principle of segregation.

MENDEL'S CONCLUSIONS

Stem height

L is the gene for stem height. It has two alleles: L (long stem) and l (short stem). L is dominant — expressed in preference to l , which is recessive ("weaker").

MENDEL'S EXPERIMENT

1 Parental (P) generation

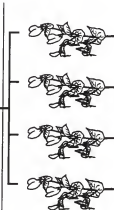
In this example, a long-stemmed pea plant was crossed with a short-stemmed one. Long stems and short stems are phenotypes (expressions) of the gene for stem height.

PHENOTYPES



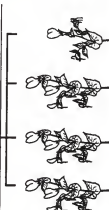
2 First (F₁) generation

All the offspring were long stemmed.



3 Second (F₂) generation

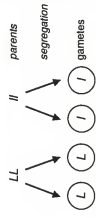
The F_1 offspring were self-pollinated. The resulting F_2 generation contained both long and short-stemmed plants.



4 Parental (P) generation

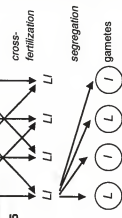
As both plants were pure breeding, each carried identical alleles. So, the long-stemmed plant had the genotype (genetic constitution) LL and the short-stemmed plant, ll . When these plants produced gametes (pollen grains), the alleles were segregated.

GENOTYPES



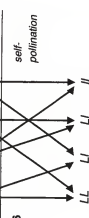
5 First (F₁) generation

Without self-pollination occurring, there is only one possible genotype for the F_1 generation: Ll . So, all the plants had a long stem. The alleles separated again to form new gametes.



6 Second (F₂) generation

When two of the F_1 gametes fused to produce new offspring, all the genotypes were possible: LL , Ll , and ll . So, the recessive phenotype of short stem reappeared.



It is now known that during meiosis (the cell division that produces gametes), pairs of homologous (matching) chromosomes separate and go to different gametes. Each chromosome of a pair.

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GREGOR MENDEL 3: PRINCIPLE OF INDEPENDENT ASSORTMENT

Mendel's principle of independent assortment states that the alleles of different genes are sorted randomly between gametes. He formulated this by studying more than one trait at a time. In the example below, the two traits being studied are seed color and seed shape.

Seed color

Y indicates the gene for seed color. It has two alleles: Y (yellow color) and y (green color). Y is dominant – expressed in preference to y , which is recessive ("weaker").

Seed shape

R indicates the gene for seed shape. It has two alleles: R (round seeds) and r (wrinkled seeds). R is dominant over recessive r .

INHERITANCE OF SEED COLOR AND SHAPE

1 Parental (P) generation

A plant with round, yellow seeds is crossed with one with wrinkled, green seeds. Both plants carry homozygous (matching) alleles for each trait. The plants produce gametes that have one allele from each pair.

2 First (F_1) generation

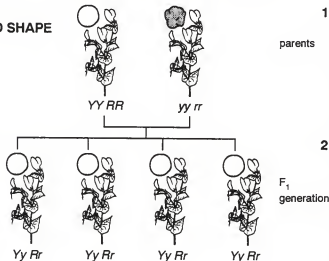
The F_1 offspring are heterozygous (carry nonmatching alleles) for both traits; so, they all have round, yellow seeds. They are dihybrids. There are four possible combinations of alleles in F_1 gametes: YR ; Yr ; yR ; and yr .

3 Second (F_2) generation

F_1 plants are crossed to produce the F_2 generation. This is called a dihybrid cross. A Punnett square is used to calculate how the F_1 gametes combine to produce the F_2 generation. Of the F_2 offspring:

- 75% have round seeds;
- 25% have wrinkled seeds;
- 75% have yellow seeds; and
- 25% have green seeds.

Overall, the ratio of phenotypes in the F_2 generation is 9:3:3:1.



		male gametes				
		YR	Yr	yR	yr	
female gametes	YR	$YY RR$	$YY Rr$	$Yy RR$	$Yy Rr$	3 F_2 generation
	Yr	$YY Rr$	$YY rr$	$Yy Rr$	$Yy rr$	
	yR	$Yy RR$	$Yy Rr$	$yy RR$	$yy Rr$	
	yr	$Yy Rr$	$Yy rr$	$yy Rr$	$yy rr$	

F_2 generation:

Proportions of color and shape

	75%	25%	
shape			
	75%	25%	
color			

Overall ratio of phenotypes

	9
	3
	3
	1

Key:

- Round, yellow seeds
- Wrinkled, yellow seeds
- Round, green seeds
- Wrinkled, green seeds

Conclusion

This ratio occurs because the genes for seed color are distributed among a plant's gametes independently from the genes for seed shape. Therefore, each combination of gametes has an equal chance of occurring. If this was not so, the ratio of phenotypes would be different. It is now known that genes on different chromosomes do behave independently of each other.

GREGOR MENDEL 4: TESTCROSSES AND BACKCROSSES

Mendel performed testcrosses to check the genotypes of offspring, which he could otherwise only assume from their appearance (phenotype) and his knowledge of their pedigree.

Principles

Plants of known genotype are crossed with those of unknown (or uncertain) genotype. The genotype of the unknown parent plant can be deduced from the offspring phenotypes.

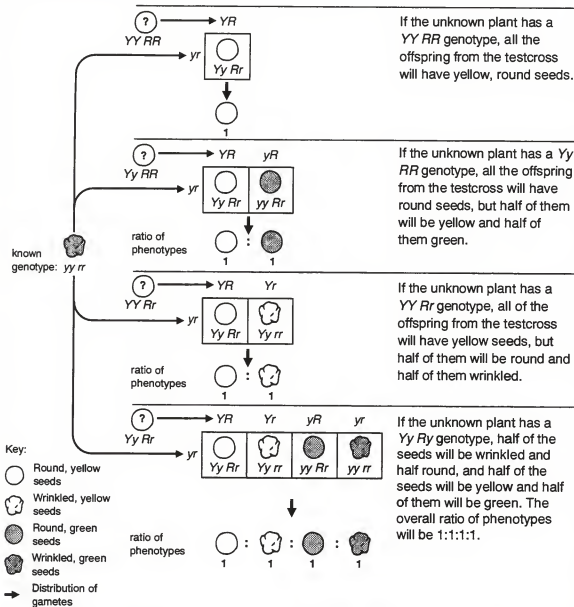
Testcross If a plant exhibits recessive phenotypes, then its genotype has to have

homozygous (matching) alleles for that trait or traits. If the unknown plant is crossed with such a recessive, then it is called a testcross.

Backcross If the recessive plant has the same genotype as the unknown plant's parents, then it is also called a backcross.

PERFORMING A TESTCROSS

In this example, the pea plant of unknown pedigree has round, yellow seeds. There is no way of telling whether its genotype is $YYRR$, $YyRR$, $YYRr$, or $YyRr$. It is crossed with a plant that has the genotype $yyrr$ – that is, it exhibits the recessive phenotypes of green and wrinkled seeds.



T. H. MORGAN AND THE CHROMOSOME THEORY OF INHERITANCE 1

In 1902, Walter Sutton (1877–1916) and Theodor Boveri (1862–1915) realized that the behavior of chromosomes during meiosis – the cell division that produces gametes (sex cells) – is similar to the behavior of Mendel's "factors." The idea that chromosomes carry the factors came to be known as the chromosome theory of inheritance. In 1910, Thomas Hunt Morgan (1866–1945) provided the first good evidence to support this theory.

MORGAN'S EXPERIMENT

Morgan knew that normal female fruit flies have two X chromosomes and males have an X and a Y chromosome.

1 Parental (P) generation

He mated a white-eyed male with a red-eyed female. White eyes and red eyes are phenotypes (expressions) of the gene for eye color.

PHENOTYPES**2 First (F₁) generation**

All the F₁ generation had red eyes.

**3 Second (F₂) generation**

When the F₁ generation flies were mated, there was a 3:1 ratio of red-eyes to white-eyes. Although half of the male flies had white eyes, however, none of the females did.



Key:
○ White eye
● Red eye



© DIAGRAM

MORGAN'S CONCLUSION

The gene for eye color was on the X (a) but not the Y (b) chromosome.

Eye color

W is the gene for eye color. It has two alleles (forms): W (red eyes) and w (white eyes). W is dominant – expressed in preference to recessive ("weaker") w.

GENOTYPES**4 Parental (P) generation**

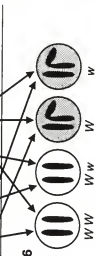
The original male fly had a single copy of the gene for white eyes (w). The female had two alleles of the gene for red eyes, giving her the genotype (genetic constitution) WW.

5 First (F₁) generation

All of the female offspring had one red-eye gene and one white-eye gene (Ww). All of the male flies had a single red-eye gene (W). All of these genotypes give red eyes.

**6 Second (F₂) generation**

Half of the F₂ males had the white-eye gene and half the red-eye gene, so half had red eyes and half had white eyes. None of the females could have had two white-eye genes, so all the females were red-eyed.



Key:
○ Male
○ Female

T. H. MORGAN AND THE CHROMOSOME THEORY OF INHERITANCE 2

Morgan performed a reciprocal ("reverse") cross to doublecheck his conclusion.

MORGAN'S EXPERIMENT

1 Parental (P) generation

He had already mated a white-eyed male with a red-eyed female; to perform the reciprocal cross for this, Morgan mated a white-eyed female with a red-eyed male.

PHENOTYPES



1

2 First (F₁) generation

The results were different from the first experiment in which all the F₁ flies had red eyes: all the males had white eyes and all the females had red eyes in this case.



2

3 Second (F₂) generation

Again, the results were different: half of both the males and females had white eyes.



3

Key:



○ White eye
● Red eye



○ Male fly
○ Female fly

MORGAN'S CONCLUSIONS

His conclusion that the gene for eye color is on the X (a) and not the Y (b) chromosome still worked. In most reciprocal crosses, the phenotypes of the offspring are the same as in the original cross. If the gene for the trait being studied is sex linked (on the X or Y chromosome) however, the results are different. This is because the Y chromosome is missing many genes.

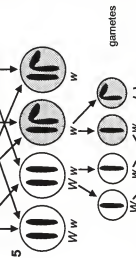
4 Parental (P) generation

The male had one allele for red eyes (W). In order to have white eyes, the female must have had identical alleles for white eyes (ww).

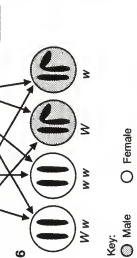
GENOTYPES

5 First (F₁) generation

The males could only inherit an eye-color gene from their mothers, so they all had white eyes. The females inherited the dominant, red-eye gene from their fathers, so they all had red eyes.

6 Second (F₂) generation

Unlike in the first experiment in which only F₂ males could have red eyes, the F₂ offspring could inherit the recessive genes from both parents. So, half of the females had white-eyes (ww).



Key:



○ Male
○ Female

DIHYBRID INHERITANCE IN FRUIT FLIES 1

Dihybrid crosses enable the study of the inheritance of more than one trait at a time. In this example, the traits being studied are fruit fly wing and bristle size. The genes for these traits are on different chromosomes.

Wing size

Vg indicates the gene for wing size. It has two alleles (forms): *Vg* (normal wings) and *vg* (miniature, or vestigial, wings). *Vg* is dominant – expressed in preference to recessive (“weaker”) *vg*.

Bristles

Ss indicates the gene for bristles. It has two alleles: *Ss* (normal bristles) and *ss* (short bristles). *Ss* is dominant over *ss*.

1 Parental (P) generation

A fruit fly with vestigial wings and small bristles (a) is mated with a fly homozygous (with matching alleles) for both normal wings and bristles (b). The genes for wing and bristle size become distributed between the gametes (the sex cells sperm and ova) that the flies produce.

2 First (F₁) generation

The F₁ generation all have normal wing size and normal bristles. This is because each fly has a dominant *Vg* and *Ss* allele. The F₁ flies are heterozygotes – they do not have identical alleles for these traits. They all have the same genotype (genetic constitution): *Vg/vg Ss/ss*.

3 Second (F₂) generation

When the flies of the F₁ generation are mated with each other, their *Vg*, *vg*, *Ss*, and *ss* genes are randomly distributed between the sex cells. A Punnett square shows how the genes in the sex cells are combined in the resulting F₂ offspring.

Of the F₂ generation:

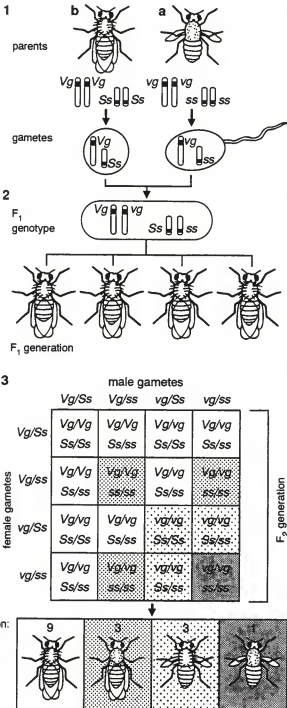
- 75% of the flies have normal wings;
- 25% have vestigial wings;
- 75% have normal bristles; and
- 25% have short bristles.

Overall, there is a 9:3:3:1 ratio of phenotypes in the F₂ generation. This is the expected ratio for traits that are determined by genes which appear on different chromosomes.

Key to Punnett square:

- Normal wings, normal bristles
- ▨ Normal wings, short bristles
- ▤ Vestigial wings, normal bristles
- ▩ Vestigial wings, short bristles

F₂ generation:
ratio of
phenotypes



DIHYBRID INHERITANCE IN FRUIT FLIES 2: TESTCROSS

A fruit fly with the dominant phenotypes of normal wings and normal bristles could have either homozygous (matching) or heterozygous (nonmatching) alleles for these traits. That is, its genotype could be: $Vg/Vg\ Ss/ss$; $Vg/vg\ Ss/Ss$; $Vg/vg\ Ss/ss$; or $Vg/Vg\ Ss/Ss$. If it was crossed with a fly homozygous for the vg and ss genes, however, then its genotype could be deduced from the phenotypes of the offspring. This is called a testcross.

Key:



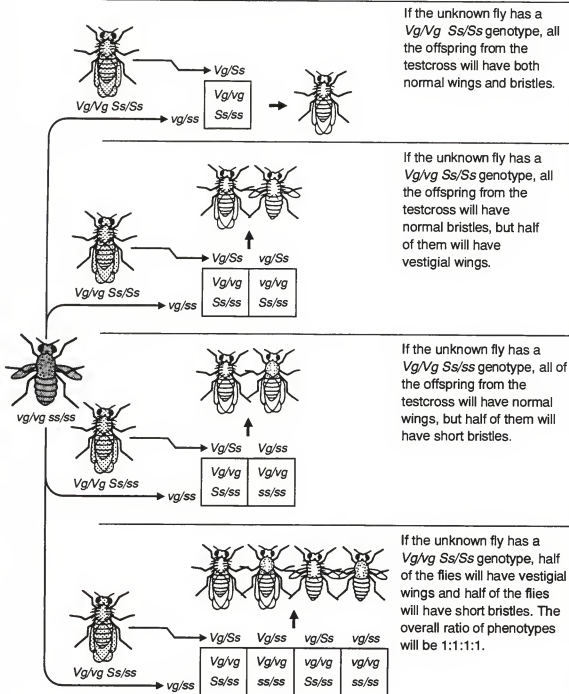
Fly of known genotype



Distribution of gametes



Fly of unknown genotype



MULTIPLE ALLELES

The different forms of a gene are called alleles. A gene that encodes for flower color, for example, may have two alleles: a purple-flower allele and a white-flower allele. If a gene has more than two forms, it is said to have multiple alleles.

ABO BLOOD GROUPS

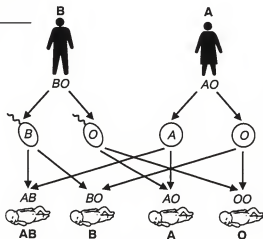
In the ABO system, the gene that determines a person's blood group has three major alleles: A, B, and O.

Inheriting a blood group

Multiple alleles are transmitted in the same way as genes that have only two alleles.

This is because no matter how many alleles a gene has, an individual can have no more than two as they occur in pairs.

Key:
A Allele
A Blood group



Genotypes and phenotypes

As a person can only inherit one allele from each parent, there are six different ways that they can combine. These are all the possible genotypes (genetic constitutions) for this trait. A person's actual blood group is their phenotype (expression) of the genes for this trait.

Key:
AO Genotype
(A) Blood group

		female gametes (ova)		
		A	B	O
male gametes (sperm)	O	AO (A)	BO (B)	OO (O)
	B	AB (AB)	BB (B)	BO (B)
	A	AA (A)	AB (AB)	AO (A)

Dominant, codominant, and recessive alleles

- **Dominant and recessive alleles** A and B alleles are dominant – they are expressed in preference to O, which is recessive (“weaker”).
- **Codominant alleles** A and B are also codominant. Each blood group has different combinations of antigens (substances that provoke an immune response) and antibodies (proteins that attack antigens). Antigens of the ABO system take two forms: A and B. The antibodies also take two forms: anti-A and anti-B antibodies. The combination of these decides which blood group a person belongs to. If a person has the alleles A and B – and therefore the blood group AB – they will have both A and B

antigens but neither antibodies. This is because A and B are codominant, meaning that both alleles are expressed when they occur together.

- Bearing these facts in mind, there are only four possible phenotypes: A, B, AB, and O.

Blood group antigens and antibodies

BLOOD GROUP	ANTIGEN	ANTIBODY
A	A	anti-B
B	B	anti-A
AB	AB	neither
O	neither	anti-A & anti-B

B. McCLINTOCK, H. CREIGHTON, AND RECOMBINATION IN CORN

In 1931, Barbara McClintock (1902–92) and Harriet Creighton (born 1909) demonstrated how homologous (matching) chromosomes in corn (*Zea mays*) can recombine, or exchange parts with each other. They studied the traits of seed endosperm (food reserve) color and waxiness.

Endosperm color

C indicates the gene for seed endosperm color. It has two alleles (forms): *C* (colored) and *c* (colorless). *C* is dominant – expressed in preference to recessive (“weaker”) *c*.

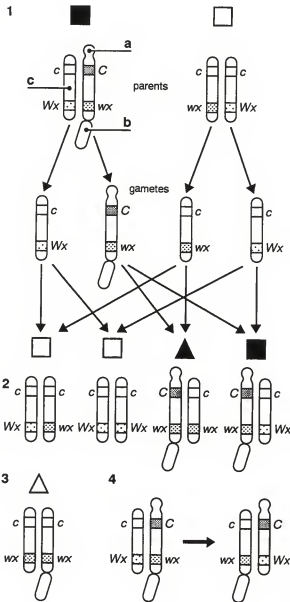
Endosperm waxiness

Wx indicates the gene for seed endosperm waxiness. It has two alleles: *Wx* (nonwaxy) and *wx* (waxy). *Wx* is dominant over *wx*.

THE EXPERIMENT

Parental (P) generation

1 McClintock and Creighton found a corn plant with an odd-looking chromosome. It had a “knob” (a) at one end and a segment (b) from a different chromosome joined onto its other end. Its homologous chromosome (c) looked normal, however. This homologous pair carried the genes for endosperm color and waxiness. The plant was heterozygous (had nonmatching alleles) for both traits and therefore had colored, nonwaxy seed endosperm. This plant was crossed with one that had colorless, nonwaxy endosperm. It had homozygous (matching) alleles for endosperm color but was heterozygous for waxiness.



First (F₁) generation

2 Theoretically, there should not have been any offspring with waxy, colorless endosperms. This is because the offspring could not inherit two *wx* (waxy) alleles without also inheriting a *C* (colored) allele.

3 A few offspring were found, however, that did have waxy, colorless endosperms. The chromosomes of these plants all seemed to have inherited the unusual chromosome, but the “knob” had been lost in the process.

4 CONCLUSION

McClintock and Creighton suggested that this could only happen if the unusual chromosome had physically recombined with its matching chromosome somehow.

Key to alleles:

Dominant Recessive

Colored Colorless

Nonwaxy Waxy

Key to phenotype symbols:

Dominant Recessive

Colored Colorless

Nonwaxy Waxy

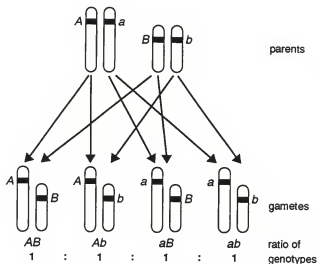
GENETIC LINKAGE 1: LINKAGE GROUPS

How combinations of genes get distributed to an organism's offspring depends on whether they are on the same or different chromosomes. If the genes are on the same chromosome, they are said to be in the same linkage group.

In these hypothetical examples, two genes are being studied: gene *A* and gene *B*. Each of these genes has two alleles (forms): *A* and *a*, and *B* and *b*. The organism in which they appear has nonmatching (heterozygous) alleles for both – it has an *Aa Bb* genotype (genetic constitution).

If the genes are on different chromosomes:

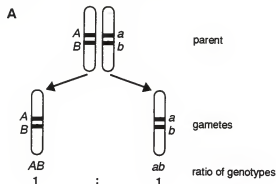
All the possible combinations of alleles occur (*AB*, *Ab*, *aB*, and *ab*) with equal probability in the gametes (sex cells). This is according to the principle of independent assortment.



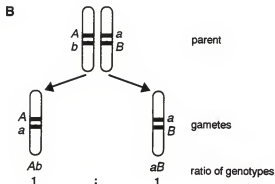
If the genes are on the same chromosome:

Independent assortment does not occur. Each homologous (matching) chromosome of a pair will have one allele of each gene. These two alleles will be passed onto the gametes together.

A If the *A* and *B* alleles are on one homologous chromosome and the *a* and *b* alleles on the other, the gametes will have either *AB* or *ab* genes. The combinations of *Ab* and *aB* cannot occur.



B If the *A* and *b* alleles are on one homologous chromosome and the *a* and *B* alleles on the other, the gametes will have either *Ab* or *aB* genes. The combinations of *AB* and *ab* cannot occur.



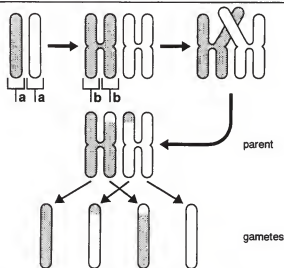
GENETIC LINKAGE 2: RECOMBINATION

MEIOSIS

Reproductive cells divide by a special form of cell division called meiosis. This produces gametes (sex cells) that have half the number of chromosomes than other cells – the n or haploid (half $2n$) amount. This ensures that when two gametes fuse on fertilization the resulting cell (the zygote) has the correct number of chromosomes – the $2n$ diploid (normal) amount.

RECOMBINATION

A cell's chromosomes (a) are first replicated so that each one consists of two identical sister chromatids (b). Before they are distributed to the gametes, the chromatids of homologous (matching) pairs of chromosomes may exchange portions with each other. This is called crossing-over or recombination. It results in the formation of recombinant chromosomes and recombinant gametes.

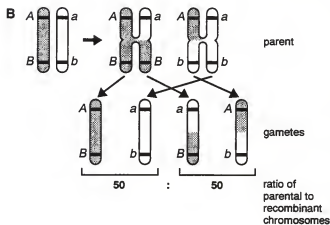
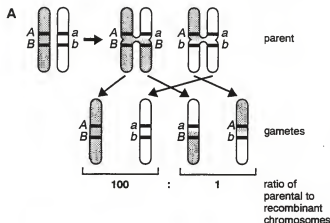


Rate of recombination

How often genes recombine depends on the physical distance between them on a chromosome.

A If two genes are close together on a chromosome, it is very unlikely that recombination will occur between them. Gametes will usually inherit the same combinations of genes that were on the parental chromosomes. There will be very few recombinant gametes.

B If two genes are not close together on a chromosome, it becomes more likely that there will be crossing-over between them. Many more recombinant gametes will be formed. The more frequently genes are shown to recombine, the greater the distance between them. If two genes are at opposite ends of the chromosome, then they behave as if they were on separate chromosomes – there is a 50% chance of the gametes being recombinants. This means that the genes are being shared between the gametes according to the principle of independent assortment.



LINKAGE MAPS

Linkage (or genetic) maps give the relative location of genes on a chromosome.

PRINCIPLES

- The genes have a known order along a chromosome.
- The "distance" (degree of linkage) between genes is statistically measured by how often recombination occurs between them.
- Recombination occurs when homologous (matching) chromosomes exchange corresponding segments. This happens during meiosis – the cell division that creates gametes (sex cells) such as ova and sperm.

CONSTRUCTING A LINKAGE MAP

The fruit fly genes for body and eye color are being mapped. They are both on chromosome 2.

Body color

B indicates the gene for body color. It has two alleles (forms): *B* (gray bodies) and *b* (black bodies). *B* is dominant – it is expressed in preference to recessive ("weaker") *b*.

Eye color

Pr indicates the gene for eye color. It has two alleles: *Pr* (red eyes) and *pr* (purple eyes). *Pr* is dominant over recessive *pr*.

1 Parental (P) generation

Two flies are crossed. One is heterozygous (has nonmatching alleles) for both traits, so it has a gray body and red eyes. The other parent is homozygous (has matching alleles) for the recessive genes, so it has a black body and purple eyes.

2 First (F₁) generation

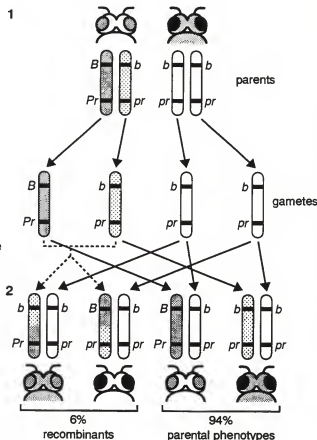
Without recombination occurring, half of the F₁ offspring would have gray bodies and red eyes and the other half would have black bodies and purple eyes. These characteristics are the same as the parental phenotypes (appearances).

In this case, however, recombination does occur. As a result:

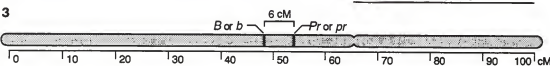
- 94% of the flies have the parental phenotypes, but
- 6% have either black bodies and red eyes or gray bodies and purple eyes. These flies must be recombinants.

3 The linkage map

This is translated into six linkage map units – each unit is 1%. These units are known as centi-Morgans (cM) after the geneticist Thomas Hunt Morgan (1866–1945).

**Key to phenotypes:**

Dominant	Recessive
Gray body	Black body
Red eyes	Purple eyes

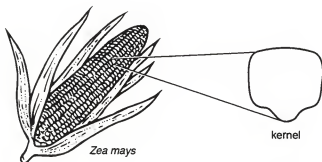


BARBARA McCLINTOCK AND JUMPING GENES

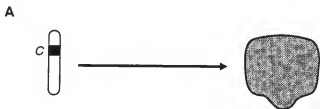
In the 1940s and 1950s, Barbara McClintock (1902–92) carried out studies on the coloration of corn (*Zea mays*). She put forward the theory that certain genes can “jump” from place to place.

KERNEL COLOR

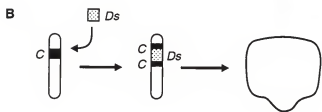
Corn kernels (seeds) can be purple or colorless. McClintock was most interested in the causes of variegation (mottling).

**A Purple kernels**

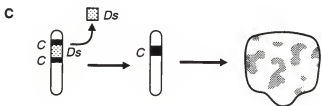
A gene called *C* causes purple-colored kernels.

**B Colorless kernels**

McClintock knew of a gene called *Ds* that could damage the chromosomes in corn. She proposed that the *Ds* gene was sometimes inserted into the *C* gene, inactivating it. This would make the kernels colorless.

**C Mottled kernels**

McClintock proposed that during the development of the colorless kernels, the *Ds* gene was somehow removed from the *C* gene in some cells. These cells would then have a functional *C* gene again and become purple. She concluded that the spots of purple color in the otherwise colorless kernels were formed by such cells.



Key:

Purple

Mottled

Most scientists were very sceptical that genes could sometimes jump out from chromosomes like this, and it was not until 1983 that direct evidence was found that these “jumping” genes really existed. Today, jumping genes are called transposable elements and they have been found in organisms ranging from bacteria to humans.

MUTATIONS

A mutation is a sudden and inheritable alteration in the cell's genetic material – its DNA (deoxyribonucleic acid). It is estimated that on average three mutations occur per each cell division. These can occur during DNA replication prior to cell division or be caused by mutagens (mutagenic agents). Examples of mutagens include:

- various kinds of radiation, including nuclear radiation, X rays, and ultraviolet (UV) light, and
- chemicals, such as the tars in tobacco smoke.

Most mutations have no noticeable effect or are corrected by the cell's machinery after they arise. Some, however, are harmful.

Types of mutation

A mutation that occurs in a reproductive cell may be passed on to the gametes (sex cells, such as ova and sperm). It will then be inherited by any offspring. A mutation that occurs in a nonreproductive cell will not be passed on to the offspring. It may, however, be

passed on to other body cells that are produced from the mutant cell by cell division. Malignant tumors (cancers) are thought to arise from mutant cells in this way.

There are two main types of mutation: gene mutations and chromosome mutations.

GENE MUTATIONS

A small-scale change in the cell's genetic material is called a gene mutation. A single gene may be affected if a small amount of genetic material is:

- a added;
- b lost;
- c rearranged; or
- d substituted.

The genetic code is based on groups of three bases called codons in the DNA (deoxyribonucleic acid). Small changes in the sequence of bases can have a major effect on their message – the triplet code – and so change the nature of the gene product (a protein). In the table on the right, three-letter words have been used to represent the base triplets (codons) in DNA.

TRIPLET CODES

Normal the old man saw the dog
(base triplets that code for the normal message)

Mutations

a the old man saw **ath** edo
(one base – “a” – has been added)

b the old **mns** awt hed ogt
(one base – “a” in “man” – has been lost)

c the old man **was** the dog
(base triplet “saw” has been rearranged)

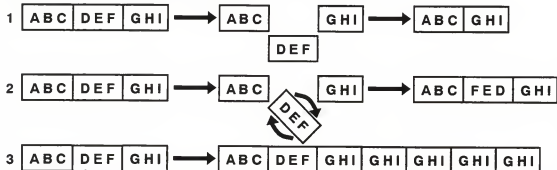
d the old man saw the **hog**
(base “d” in “dog” has been substituted by “h”)

CHROMOSOME MUTATIONS

A large-scale change in the cell's genetic material that affects several genes, or even an entire chromosome, is a chromosome mutation. Some of the genes (represented

below by letters) in the chromosome may be:

- 1 deleted;
- 2 rearranged; or
- 3 duplicated.



GENE MUTATIONS

Diseases or conditions that are inherited are called genetic disorders. Some of the most common of these are caused by gene mutations (small-scale alterations in the cell's genetic material). About 20% of the more than 50,000 human genes have different forms (alleles). Much of this variation probably does not affect the survival of the individual. Each person is probably a carrier of half a dozen recessive alleles for a severe disease. These alleles are only expressed if an individual is homozygous (has identical paired alleles) for the disease.

1 CYSTIC FIBROSIS

The gene mutation affects the mucous glands of the body, causing them to produce mucus (thick, slimy fluid) that is thicker than normal.

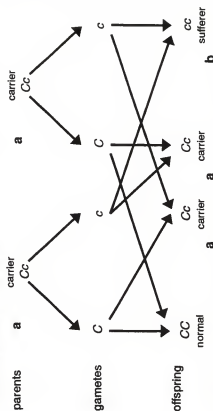
Effect on the lungs

Breathing and gas exchange are impaired and infections such as pneumonia are more likely.

Genotype and cystic fibrosis

Cystic fibrosis is caused by a recessive allele (c). Heterozygous individuals (Cc) (a), although carriers, will be healthy because the normal allele is dominant. Homozygous individuals (cc) (b) will actually have the disease.

1 Inheritance of cystic fibrosis



2 SICKLE-CELL ANEMIA

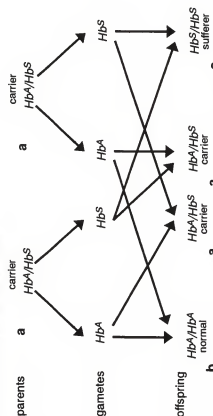
The gene mutation results in an abnormal form of hemoglobin (oxygen-carrying pigment) being made in red blood cells. The cells become sickle shaped and fragile. This reduces the blood's oxygen-carrying capacity (a condition called anemia).

heterozygous (Hb^A/Hb^S) (a), homozygous for the normal allele (Hb^A/Hb^A) (b), or homozygous for the sickle-cell allele (Hb^S/Hb^S) (c). Heterozygous individuals have some abnormal hemoglobin and are said to carry the sickle-cell trait. This is not normally serious. It is the homozygous individuals who suffer from severe anemia.

Genotype and sickle-cell anemia

In communities where the disease occurs, individuals are

2 Inheritance of sickle-cell anemia

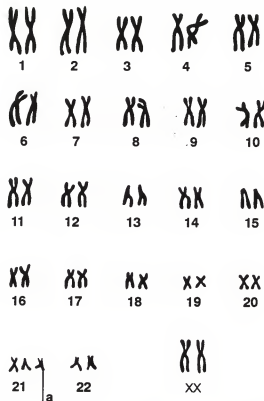


CHROMOSOME MUTATIONS

There are several conditions that can afflict humans in which an incorrect number of chromosomes is inherited by offspring. These conditions are caused by a mistake during meiosis – the cell division that leads to the formation of the gametes (sex cells) ova or sperm.

DOWN'S SYNDROME

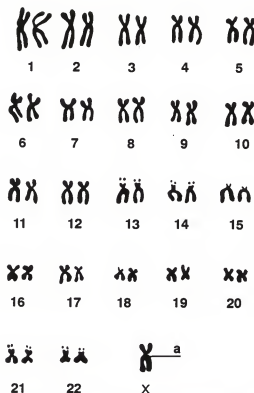
This condition is caused by an extra chromosome (a) in the 21st pair, so that the individual has 47 chromosomes instead of the normal 46. Although the extra chromosome can come from either parent, the risk of having an affected child does rise with the age of the mother. For women in their twenties, the figure is about 1 in 2,000; the risk rises at the age of 32 and reaches a maximum of more than 1 in 50 for women aged 45 or older.

**Characteristics**

People who are affected by this syndrome have characteristic facial features and physique. They are prone to heart disease and intestinal problems. They have reduced intellectual powers and tend to be childlike and affectionate.

TURNER'S SYNDROME

In Turner's syndrome, the individual has a single X chromosome (a) and lacks a second sex chromosome. The individual's sexual genotype (genetic constitution) is XO. Normally, a person is either XX (female) or XY (male).

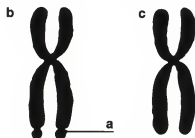
**Characteristics**

The condition results in certain characteristic physical features. The person is recognizably female in appearance but has incomplete sexual development and is infertile.

FRAGILE X SYNDROME

FRAGILE X CHROMOSOMES

A region (a) of a fragile X chromosome (b) is greatly narrowed, so it almost appears to be missing; it is also slightly longer than normal. This is because a very small segment of the chromosome has been repeated many times more than is usual. Normal X chromosomes (c) have around 5–50 repeats of this segment; fragile X chromosomes have 200–1,300 repeats.



FRAGILE X SYNDROME

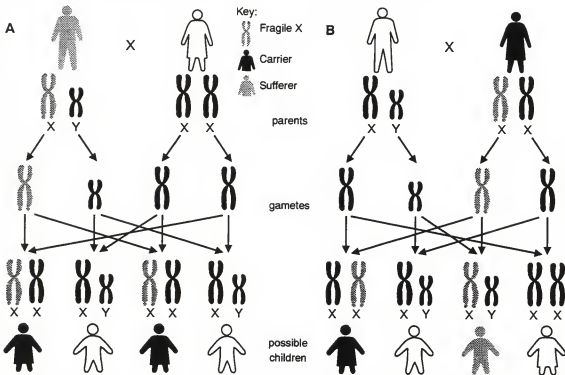
People with fragile X syndrome are educationally subnormal (mentally retarded). Physically, they are often tall, strong, and might have a large nose and jaw.

- 1 in 1,250 men have fragile X syndrome compared to 1 in 2,500 women.
- Men are afflicted more than women because they do not have another X chromosome to mask the effects of the mutated one.
- 20% of men who have the fragile X chromosome do not develop the syndrome. They are, effectively, carriers.

Inheritance of fragile X syndrome

A A man who has a fragile X chromosome (whether he is a sufferer or not) will transmit it to any daughters but not to his sons. These daughters become carriers.

B A daughter of a woman who is carrier has a 1 in 2 (50%) chance of becoming a carrier. A son has a 1 in 2 chance of receiving a fragile X chromosome.

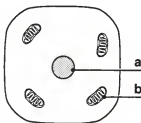


Amplification

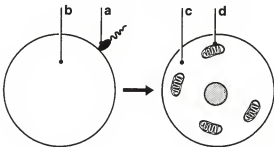
The number of the repeats in the X chromosome can increase (amplify) through generations. A father with mild mental retardation will probably have a daughter of normal mental abilities. This daughter, however, can have a son with very severe fragile X syndrome: the number of repeats in the X chromosome has increased. This amplification only occurs in women, not men.

MITOCHONDRIA AND MATERNAL INHERITANCE

Cells of eukaryotic organisms, such as plants and animals, contain organelles (miniorgans) called mitochondria. Almost all of a cell's genetic material – DNA (deoxyribonucleic acid) – is found in the nucleus (control center) (a). A small amount, however, is also found inside the mitochondria (b). It is called mtDNA (mitochondrial DNA).

**Inheritance of mitochondria**

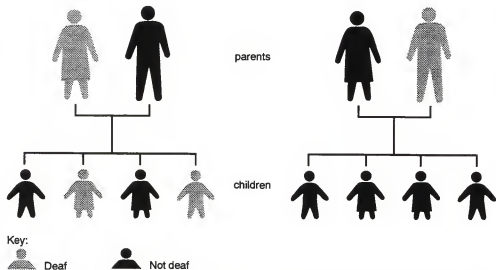
In sexual reproduction, a male gamete (sex cell) such as a sperm (a) fertilizes a female gamete (such as an ovum) (b). The resulting zygote (fertilized cell) (c) contains only mitochondria (d) that came from the female gamete. No mitochondria from the male gamete are passed on to the zygote. This is called maternal inheritance.

**Deafness**

One human condition that is caused by a genetic defect of mitochondrial DNA is deafness.

A If a deaf woman has children with a man who has normal hearing, then their children can inherit the deafness. The mother passes on her defective mitochondria to her offspring.

B If a deaf man has children with a woman who has normal hearing, then the children cannot inherit the deafness. This is because the father does not pass on his mitochondria to his children.



SEX DETERMINATION 1: Y-CHROMOSOME MECHANISM

SEX CHROMOSOMES OF MAMMALS

In mammals, one of the pairs of homologous (matching) chromosomes – the sex chromosomes – is responsible for determining the sex of an individual. The sex chromosomes exist in two forms, X and Y, so called because of their characteristic shape during cell division.

A Female sex chromosomes

Female sex chromosomes are both X, giving the individual the sexual genotype (genetic constitution) XX.

**B Male sex chromosomes**

One male sex chromosome is an X and the other is a Y, giving the individual the sexual genotype XY.

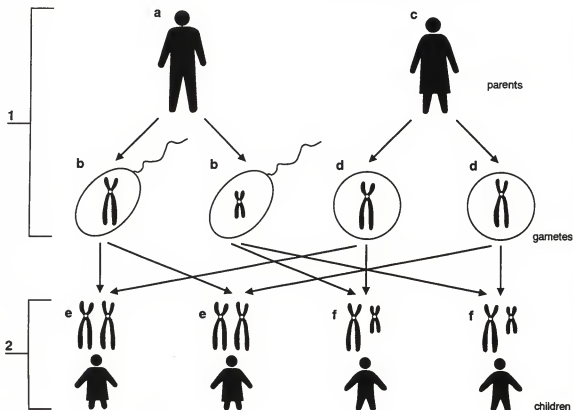


HOW SEX IS DETERMINED

In the Y-chromosome mechanism of sex determination, the presence or absence of the Y chromosome determines sex. This occurs in mammals and some plants and insects.

1 A male (a) produces gametes (sperm) (b) which may contain, with equal probability, either an X or a Y chromosome. A female (c) produces gametes (ova) (d) which always carry an X chromosome.

2 When a sperm and ovum fuse at fertilization, the sex of the resulting offspring is determined by the type of sex chromosome passed on in the father's sperm. Therefore, there is an equal probability that offspring will be female (e) or male (f).



SEX DETERMINATION 2: X CHROMOSOME-AUTOSOME BALANCE

In some organisms, sex is determined not by the presence or absence of Y, but by the ratio of X chromosomes to sets of autosomes (nonsex chromosomes). This is called the X chromosome-autosome balance system of sex determination. It occurs in fruit flies and some higher plants.

FRUIT FLY SEX CHROMOSOMES

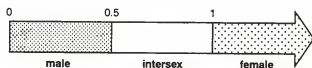
Fruit flies have eight chromosomes, which fall into four homologous (matching) pairs: three pairs of autosomes and one pair of sex chromosomes. The sex chromosomes take two forms: X and Y. They are of similar height, but the Y chromosome is hook shaped.



HOW SEX IS DETERMINED

If the ratio of X chromosomes to sets of autosomes is:

- 0.50 or under, the fly is a male;
- between 0.50 and 1.00 the fly is an intersex fly (it has a mix of male and female sex organs); or
- 1.00 or over, the fly is female.

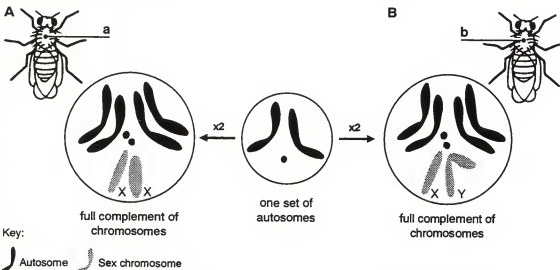


A Normal female chromosomes

A normal female (a) has two X chromosomes and two sets of autosomes, giving a ratio of 2:2 or 1. (One set comprises one chromosome from each homologous pair.)

B Normal male chromosomes

A normal male (b) has an X and a Y chromosome and two sets of autosomes. This gives a ratio of 1:2 or 0.50.



C Intersex and other mutant flies

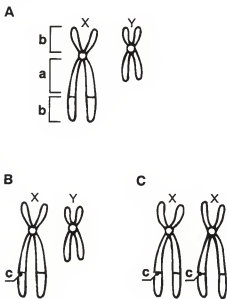
Mistakes during meiosis can lead to a fly having more, or sometimes fewer, chromosomes than normal. The sex of these flies still follows the same rules, but most are sterile.

Sex chromosomes	Sets of autosomes (A)	Ratio of X:A	Sex of fly	Sterile
X	2	1:2 or 0.50	male	✓
XX	3	2:3 or 0.67	intersex	✓
XXX	4	3:4 or 0.75	intersex	✓
XXY	2	2:2 or 1.00	female	✗

HUMAN SEX-LINKED GENES AND GENETIC DISORDERS 1

A SEX-LINKED GENES

Like other chromosomes, the sex chromosomes carry genes. A human male has the sexual genotype XY – his cells contain an X chromosome and a Y chromosome. Some parts of the X chromosome are homologous (matching) (a) with parts of the Y chromosome, while other parts are not. Nonmatching regions of the X chromosome are called nonhomologous portions (b). Genes on these parts are said to be sex linked. Whether an individual expresses these genes or not depends on the combination of sex chromosomes he or she has.



Recessive gene expression

Recessive sex-linked alleles (gene forms) are more commonly expressed in males than in females.

B In a male If a recessive allele (c) is present on a nonhomologous portion of the X chromosome, the allele will be expressed because there is no allele present on the Y chromosome that could mask it.

C In a female A female has the sexual genotype XX and so must have two copies of a recessive allele (c) for the recessive characteristic to be expressed.

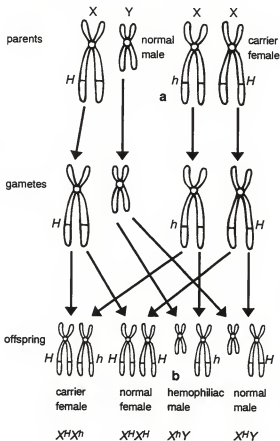
SEX-LINKED GENETIC DISORDERS

Hemophilia

A person with hemophilia lacks a protein needed to make blood clot quickly, and a minor injury may result in profuse bleeding that is life threatening. Certain forms of hemophilia are sex linked and are caused by a recessive allele (*h*) on the X chromosome.

Inheriting hemophilia A woman with a single hemophilia allele (genotype $X^H X^h$) (a) is a carrier for hemophilia, but she does not have the condition herself. Her second X chromosome bears a normal allele (*H*) which codes for the vital blood-clotting protein. A man with the hemophilia allele (genotype $X^h Y$) (b) has no second X chromosome. Therefore, his hemophilia allele will be expressed and he will have the condition.

Hemophiliac females For a woman to suffer from hemophilia, she would need to be homozygous ($X^h X^h$) for the hemophilia allele – she inherits the allele from both her parents. This is less likely to occur than inheriting one allele and is the reason why fewer women than men suffer from hemophilia.



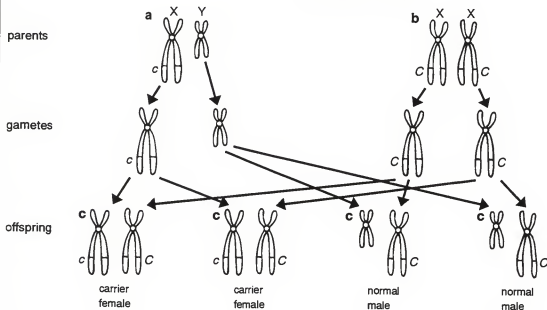
HUMAN SEX-LINKED GENES AND GENETIC DISORDERS 2

Red-green colorblindness

Red-green colorblindness is a relatively common condition in men. It is caused by a recessive allele (c) located on the nonhomologous portion of the X chromosome.

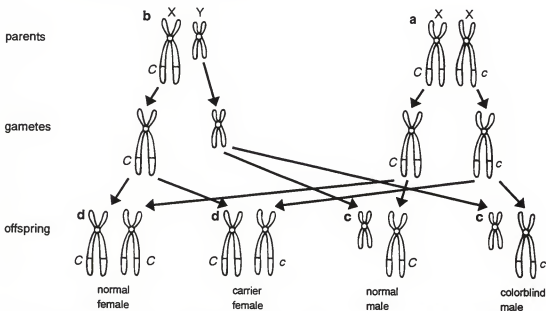
Inheriting colorblindness from a male

A colorblind man (X^cY) (a) and a woman homozygous for normal color vision (X^CX^C) (b) will produce children (c) with normal color vision. All the female children, however, will be carriers (X^CX^c).

**Inheriting colorblindness from a female**

A female carrier (a) and a male who has normal color vision (b) will produce normal or colorblind male offspring (c). The female children (d) will either have normal color vision or be carriers of the colorblindness allele.

Colorblind females Girls can only be colorblind if they inherit an X chromosome with an allele for colorblindness from both their mother and their father – a rare occurrence.



EPISTASIS

Two or more genes acting together to produce a particular characteristic (such as purple flowers) is called epistasis. In this example, the trait being studied is flower color in sweet peas.

Flower color

In sweet peas, flower color is determined by two genes, *C* and *P*. These genes both have two alleles (forms): *C* (colored) and *c* (colorless); *P* (purple) and *p* (white). *C* and *P* are dominant – expressed in preference to the recessive (“weaker”) forms of *c* and *p* respectively.

Purple flowers The plants need a dominant allele of both genes to be able to have purple flowers – that is those with the genotype (genetic constitution): *CC PP*, *Cc PP*, *CC Pp*; or *Cc Pp* will have purple flowers.

White flowers Plants that lack a *C* or a *P* allele will have white flowers.

HOW FLOWER COLOR IS INHERITED**1 Parental (P) generation**

A pure-breeding, white-flowered plant lacking a *C* allele is crossed with a pure-breeding, white-flowered plant that lacks a *P* allele.

2 First (F₁) generation

The F₁ offspring all have purple flowers because they each have a copy of both the *C* allele and the *P* allele. These are called dihybrids.

3 Second (F₂) generation

The F₁ offspring are cross-fertilized to produce the F₂ offspring. This is called a dihybrid cross. A Punnett square is used to calculate how the F₁ gametes (pollen grains) combine to produce the F₂ offspring. The F₂ generation includes plants of both phenotypes (white or purple flowers). The ratio of purple flowers to white flowers is found to be 9:7.

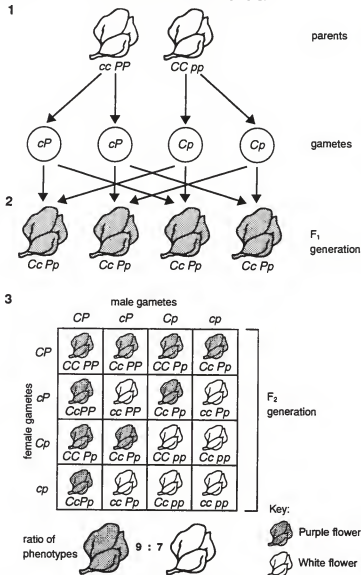
Conclusion

Dihybrid crosses involving two genes normally produce a phenotype ratio of 9:3:3:1. This happens if the two genes being studied:

- are independently sorted between gametes (they occur on different chromosomes), and
- they affect different traits (seed color and

seed shape, for example).

The 9:7 ratio of phenotypes in this F₂ generation occurs, however, because although the two genes being studied segregate independently, both have an effect on the same trait: flower color.



PLEIOTROPY

The ability of a gene to affect an organism in many different ways is called pleiotropy. If one part of an organism's metabolism is affected by a defective gene, there may be many knock-on effects. All the symptoms that result can be wide-ranging and might, initially, seem unconnected.

SICKLE-CELL ANEMIA

An example of pleiotropy is given by the disease of sickle-cell anemia.

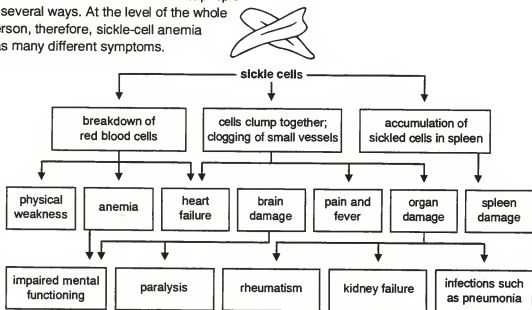
Red blood cells

Normal, healthy red blood cells (a) have a characteristic disk shape. They contain hemoglobin (b), which is the protein that transports the vital gas oxygen around the body.

Hemoglobin S The gene for hemoglobin is slightly different in people with sickle-cell anemia. As a result, sufferers have a different type of hemoglobin, called hemoglobin S (c). When molecules of hemoglobin S are not carrying oxygen, they have a tendency to form long chains. These chains deform the red blood cells into a sickle shape (d).

**Symptoms**

The deformed red blood cells affect people in several ways. At the level of the whole person, therefore, sickle-cell anemia has many different symptoms.



POLYPOIDY

Diploid eukaryotic organisms (such as many plants and animals) have two sets of chromosomes. Humans, for example, have 46 chromosomes which fall into 23 homologous (matching) pairs. One set – 23 chromosomes, one chromosome from each homologous pair – is derived from the mother and the other from the father. Some organisms, however, have more than two sets of chromosomes. This is called polyploidy.

POLYPOIDY IN PLANTS

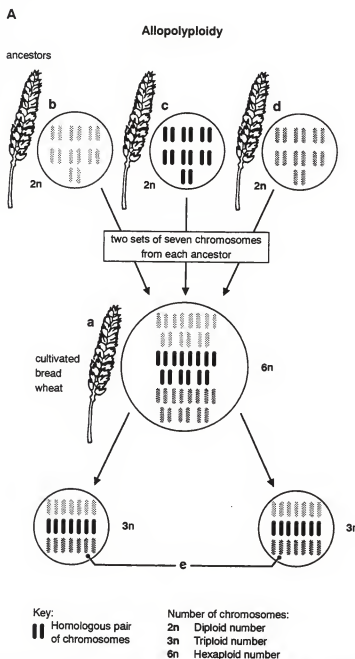
Polyploidy can occur as a result of mistakes during meiosis – the cell division that produces gametes (sex cells). It can also be engineered with the use of the chemical colchicine, which disrupts meiosis. Either way, offspring inherit two or more sets of chromosomes from one or both parents. This is usually lethal to animals, but can be tolerated by plants.

Autopolyploidy

In this type of polyploidy, all the chromosome sets are from the same species. The cultivated banana is an example of an autopolyploid. It is a triploid organism as it has three sets of chromosomes. Organisms with odd numbers of chromosome sets are usually sterile. In plants, this means large, seedless fruits (such as the banana) are produced. New banana plants are grown from cuttings.

A Allopolyploidy

In this type of polyploidy, the chromosome sets come from different species. Cultivated bread wheat (a) is a natural allopolyploid. It has 42 chromosomes, which fall into six sets of seven, making it a hexaploid. Bread wheat is thought to descend from three diploid ancestors (b, c, and d), each of which contributed two sets of seven chromosomes. As it has an even number of chromosome sets, this wheat is fertile. It produces gametes (e) with 21 chromosomes each.



GENETIC COUNSELING 1

Genetic counseling analyzes the risk that a person has a genetic defect or that couple will have a child with a genetic disorder. The counselor then informs the client what this means.

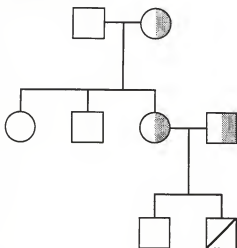
WHO IS COUNSELED?

- Those who have a disease that is known (or suspected) to be inherited.
- People who have a close relative who has a disease that is known (or suspected) to be inherited.
- Parents of a child with a birth defect.
- Women having children later in life. After they reach 32, women have a higher chance of giving birth to a baby with birth defects such as Down's syndrome.
- People who have been exposed to agents, such as radiation and certain chemical compounds (including some drugs), that can cause birth defects.
- Pregnant women who have been exposed to viruses (such as German measles) that can cause birth defects.
- Close relatives who are planning to have children. The children of parents who are first cousins have a two to three times higher risk of having birth defects than the children of unrelated parents.

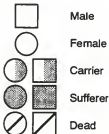
THE GENETIC COUNSELOR'S ROLE**1 Risk assessment**

The first task is to assess the likelihood that a person has a genetic defect or that a couple will have a child with a genetic disorder. This can involve pedigree analysis and, or, genetic screening.

Pedigree of a family with a history of sickle-cell anemia.

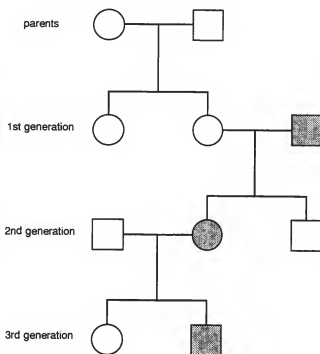


Key:



Pedigree analysis can help determine if a genetic disease is present in someone's family history. Sometimes, the genotypes (genetic constitutions) of individuals can be deduced from a pedigree.

Pedigree of a family with a history of Huntington's disease.



(continued on 5.32)

© DIAGRAM

GENETIC COUNSELING 2

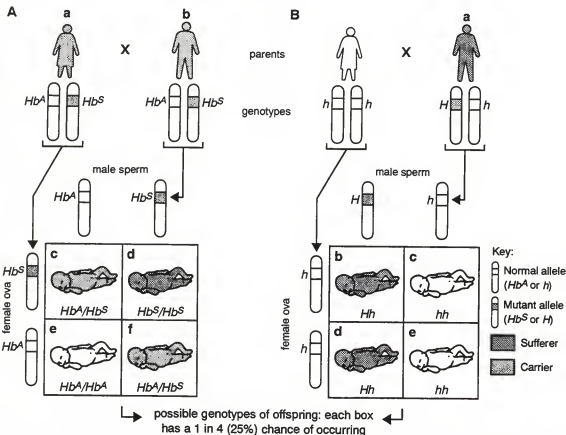
1 Risk assessment (continued from 5.31)

Genetic screening Blood tests, DNA tests, and other techniques can determine a person's genotype for a disease.

A Recessive genetic diseases – such as sickle-cell anemia – are only exhibited by people who carry two copies (alleles) of the responsible mutant gene (Hb^S). A carrier has just one mutant allele and will not develop the disease. If both parents (a and b) are carriers, however, there is a:

- 2 in 4 (50%) chance (c plus f) that a child is a carrier;
- 1 in 4 (25%) chance (d) that the baby will inherit two mutant alleles and develop the disease; and
- 1 in 4 chance (e) that a child will be normal.

B Other genetic disorders – such as Huntington's disease – are dominant traits. An individual needs to have only one allele (H) to develop the disease. As this disease does not manifest itself until in later life, a person could have the gene and not be aware of it. The children of someone (a) with a dominant genetic disease have a 2 in 4 (50%) chance (b plus d) of inheriting the gene.

**When is genetic screening useful?**

- The test must be accurate.
 - There is an affordable genetic test available.
 - The test is socially and ethically acceptable.
- For example, tests should only be carried out with the permission of the people being tested. A person should never be forced into

taking a test or taking a particular action based on the outcome of the test.

- The test results should be confidential. A controversial issue regarding this is whether or not health insurance companies should be allowed to know the results of tests.

(continued on 5.33)

GENETIC COUNSELING 3

(continued from 5.32)

2 Fetal testing

If there is a risk that a fetus has a genetic defect, then tests can be done to confirm whether or not it is affected. Testing for Down's syndrome is routine for women over the age of 35.

A Amniocentesis

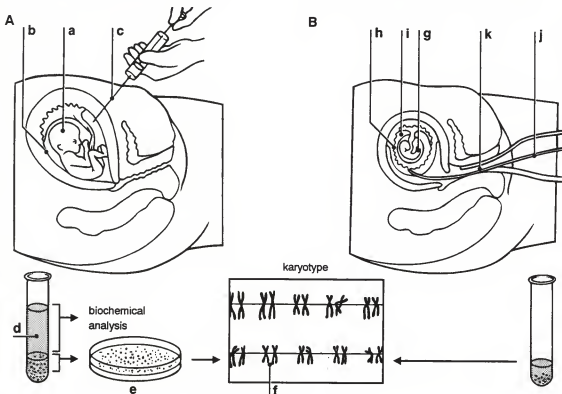
This test is not usually done until at least the twelfth week of pregnancy.

- Ultrasound is used to locate the fetus (a) and the amniotic sac (bag of fluid that surrounds the fetus) (b).
- A needle (c) is inserted into the amniotic sac and a sample of amniotic fluid (d) is taken.
- This fluid contains cells that have been shed by the fetus. They are cultured (e) and their genetic make-up tested for disorders. The chromosomes (f) can be karyotyped (sorted) to check for chromosomal abnormalities such as Down's syndrome.
- The fluid is tested for abnormal quantities of enzymes (biological catalysts) and other proteins related to certain conditions.

B Chorionic villi sampling (CVS)

This test can be done as early as eight weeks, but is usually not done before ten weeks. The results are obtained faster than in amniocentesis.

- Ultrasound is used to locate the fetus (g) and the chorion (h) – the inner surface of the placenta (i).
- Samples are taken of the chorionic villi (fingerlike projections). This can be done via a tube (j) inserted into the vagina (k) or through a needle as in amniocentesis.
- The chorion is made of cells that have the same genetic make-up as the fetus. These cells do not need to be cultured and can be tested for genetic defects and karyotyped for chromosomal abnormalities immediately.

**Risks of fetal testing**

Both tests slightly increase the risk of miscarriage, CVS more so than amniocentesis. There is also a risk of injuring the fetus, though ultrasound has lessened this. In particular, finger and toe defects are associated with CVS. There is also a risk of inaccurate diagnosis due to the presence of the mother's cells in a sample. This is more common in CVS.

(continued on 5.34)

GENETIC COUNSELING 4

(continued from 5.33)

3 Informing the clients

It is vital that people understand what their risk assessment and the results of any fetal tests mean.

Facts that they will need to know include:

- The medical facts about a disease: its probable development, symptoms, and progression.
- What treatment is available. Although most genetic diseases are incurable, sometimes treatment can alleviate the symptoms.
- How certain it is that the disease will develop. For example, women who have one of the genes associated with breast cancer will not necessarily develop breast cancer; many women who do not have the gene, however, do develop the cancer.

4 Dealing with the information

The final decision on what to do with this information can only be made by the clients. The genetic counselor can, however, inform them of various options:

- A couple might decide not to have children if there is a high chance that their child will be affected by an inherited disease. Instead, they could adopt children or try artificial insemination (the mother's egg is fertilized by a healthy donor sperm).
- A woman already expecting may decide to have an abortion if the fetus is abnormal.

TWO EXAMPLES OF GENETIC COUNSELING PROGRAMS**Tay-Sachs disease**

This disease causes newborn babies to suffer from progressive paralysis, blindness, and deafness. Babies that have the disease usually die by the age of about three years old. Tay-Sachs is caused by a recessive allele and it is most common in Ashkenazie Jews.

Screening for Tay-Sachs An expectant father is tested for how much of an enzyme called hexosaminidase A he has in his blood. The results determine whether the father is a carrier of the disease. If he does not carry the disease, then the mother and unborn child are not tested. If the father is found to be a carrier, the mother is tested. If the mother is a carrier, the fetus is tested to see if it is affected by the disease. If the fetus tests positive, then the parents can decide whether or not to abort. Voluntary screening programs organized by Jewish communities have reduced the incidence of the disease in North America by more than 70%.

Tay-Sachs

- 1/25,000 Ashkenazie Jews are sufferers
- 1/25 Ashkenazie Jews are carriers
- 1/250,000 affected in other groups

Sickle-cell anemia

This disease is caused by a recessive mutant of the hemoglobin gene. Hemoglobin is the protein in red blood cells that carries oxygen around the body. Infants often die from the disease because they are prone to bacterial infections, though the number of deaths can be reduced by antibiotics. Sickle-cell anemia is most common among people of African descent and, to a lesser degree, among people of Mediterranean descent.

Screening for sickle-cell anemia In the early 1970s, nationwide screening programs were set up in the United States. Many states made the testing of African-Americans compulsory. The screening programs were not backed up with counseling, however, and many people who were only carriers assumed they had the disease. Furthermore, some carriers were denied health insurance after the results of their tests were not kept confidential. Racial tensions developed, and the compulsory screening programs were abandoned.

Sickle-cell anemia

- 150/100,000 African-Americans are sufferers
- 1/12 African-Americans are carriers

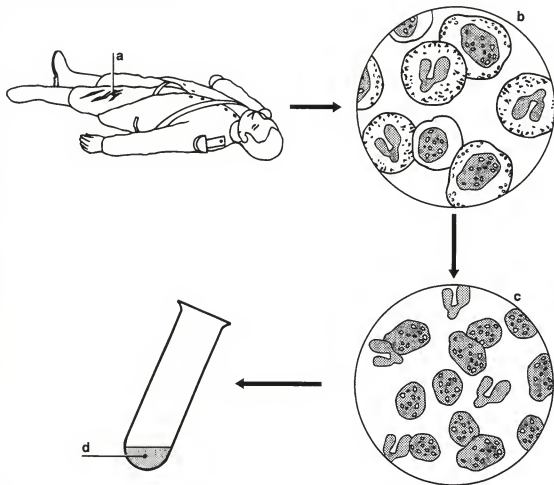


FRIEDRICH MIESCHER AND THE DISCOVERY OF NUCLEIC ACIDS

In 1869, Friedrich Miescher (1844–95) discovered "nuclein." By 1940, it was known that nuclein consisted of two types of nucleic acid: DNA (deoxyribonucleic acid) and RNA (ribonucleic acid). Miescher's discovery was one of the first major breakthroughs in understanding the chemical nature of genes, which are now known to be made of DNA.

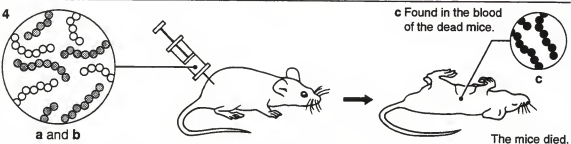
DISCOVERY OF NUCLEIN

From the pus in the wounds of a dead soldier (a), white blood cells (b) were taken and their nuclei (control centers) (c) isolated. Nuclein (d), a phosphorus-containing organic mixture, was purified from these nuclei.



FREDERICK GRIFFITH AND BACTERIAL TRANSFORMATION

Bacterial transformation was first reported by Frederick Griffith (c. 1879–1941) in 1928. His first three experiments (1, 2, and 3) were carried out as controls. The results show that the mice were unaffected by the heat-killed strain of bacteria (a) and the nonvirulent strain of bacteria (b), but died when injected with the living, virulent strain of bacteria (c). In the critical experiment (4), the mice were injected with the two strains of bacteria that did not cause death when administered alone. In this experiment, however, the mice died. The presence of the living, virulent strain of bacteria in their blood and tissues allowed Griffith to conclude that the nonvirulent strain of bacteria had somehow been transformed into the virulent form and this had killed the mice. Until the work of Oswald Avery and colleagues in 1944, it was not known, however, what the transforming agent was (see 6.03).

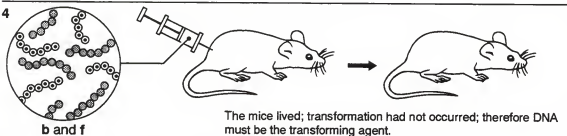
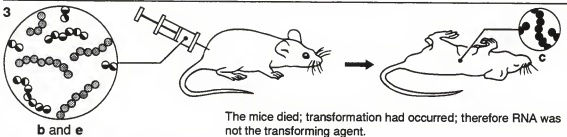
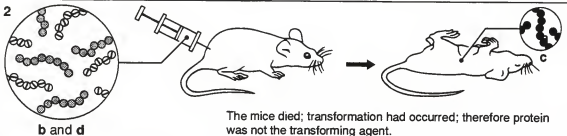
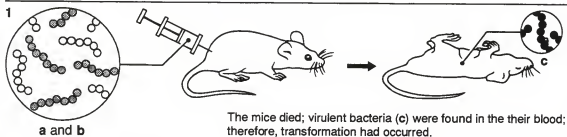


Key:

- Heat-killed S strain *Streptococcus pneumoniae* (a)
- Live R strain (nonvirulent) *Streptococcus pneumoniae* (b)
- Live S strain (virulent) *Streptococcus pneumoniae* (c)

OSWALD AVERY AND CO-WORKERS: GENES CONSIST OF DNA

In 1928, Frederick Griffith reported on the phenomenon of bacterial transformation (see 6.02) by showing a nonvirulent strain of bacteria (a) becoming virulent (1). In 1944, Oswald Avery (1877–1955) and his co-workers were able to establish that the transforming agent was DNA (deoxyribonucleic acid), and not RNA (ribonucleic acid) or protein, by seeing if transformation occurred when either the viral protein (2), RNA (3), or DNA (4) was destroyed.



Key:

- ○ ○ ○ ○ Heat-killed S strain *Streptococcus pneumoniae* (a)
- ● ● ● ● Live R strain (nonvirulent) *Streptococcus pneumoniae* (b)
- ● ● ● ● Live S strain (virulent) *Streptococcus pneumoniae* (c)
- ○ ○ ○ ○ Heat-killed S strain treated to destroy all proteins (d)
- ○ ○ ○ ○ Heat-killed S strain treated to destroy all RNA (e)
- ○ ○ ○ ○ Heat-killed S strain treated to destroy all DNA (f)

Avery and his team then took DNA from one type of bacteria and introduced it into the cells of another type of bacteria, which began to pass on certain hereditary traits identical to those of the bacteria from which the DNA had come. Avery and his co-workers assumed that genes must have been transferred from one type of bacteria to the other. As the only part of the bacteria transferred was the DNA, this provided the first convincing proof that genes are carried by DNA.

BEADLE, TATUM, AND THE ONE GENE, ONE ENZYME THEORY 1

A clue to the functioning of genes came from the early twentieth-century work of Archibald Garrod (1857–1936). In studying a rare human disease that seemed to be inherited as a recessive trait, Garrod speculated that it arose from the lack of a specific enzyme (biological catalyst). Implicit in his work was the relationship between genes and enzymes. It was not until 1941, however, that this relationship was precisely formulated as the "one gene, one enzyme" theory by George Beadle (1903–89) and Edward Tatum (1909–75). This theory proposed that each gene carries the information for building a particular enzyme.

The theory was later modified to "one gene, one polypeptide chain." It was discovered that some enzymes require the presence of more than one gene to be produced and not all gene products are enzymes.

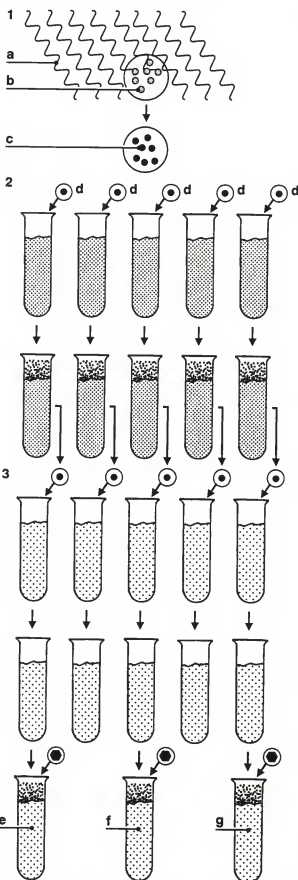
BEFORE THE EXPERIMENT

- 1 Using X rays (a), *Neurospora* (bread mold) cells (b) were mutated to produce mutagenized cells (c).
- 2 Individual spores (reproductive bodies) (d) of the mutated strain were germinated in complete (nutrient-rich) media.
- 3 Spores from each culture were then tested in minimal (nutrient-deficient) media. Of the hundreds of cultures grown, some mutant spores could not grow in this media unless the amino acid (protein building block) arginine was added. This meant that Beadle and Tatum had isolated strains of *Neurospora* (e, f, and g) that could not make their own arginine.

(continued on 6.05)

Key:

- Arginine molecule
- ▨ Complete media
- ▤ Minimal media
- ⬆ Bubbles indicate that *Neurospora* is growing



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BEADLE, TATUM, AND THE ONE GENE, ONE ENZYME THEORY 2

(continued from 6.04)

4 THE EXPERIMENT

The three different mutant *Neurospora* (e, f, and g) were grown in minimal media. Various nutrients were added to each to see if molecules other than arginine would allow them to grow. Of the three mutant strains:

- one (e) could grow with either ornithine, citrulline, or arginine;
- another (f) could grow with citrulline or arginine; and
- the last (g) could only grow with arginine.

5 DEDUCED BIOCHEMICAL PATHWAY

Each mutant was defective in one gene (h, i, or j) whose product – an enzyme (k, l, or m) – triggers a step in the biochemical pathway leading to the production of arginine.

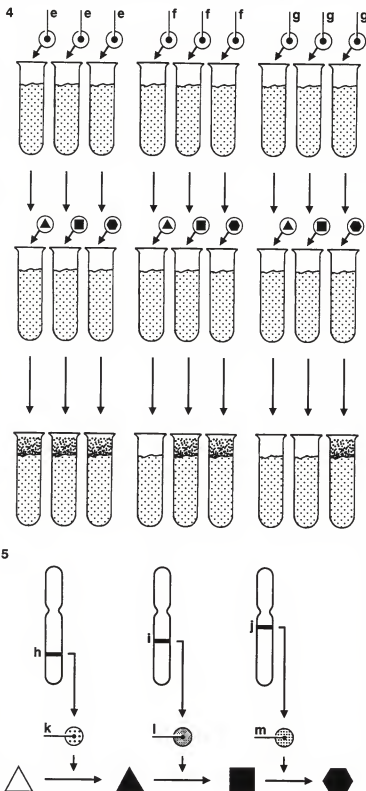
- One mutant (e) could not produce an enzyme (k) as it lacked the necessary gene (h). As this enzyme is at the beginning of the pathway, however, the mutant could grow if either arginine, citrulline, or ornithine was added.
- Another mutant (f) could not produce a different enzyme (l) as it lacked the necessary gene (i). As this enzyme is in the middle of the pathway, the mutant needed either citrulline or arginine to grow.
- The last mutant (g) also could not produce an enzyme (m) as it lacked the right gene (j). As this enzyme is at the end of the pathway, the mutant could only grow with arginine.

Key:

- Arginine molecule
- ▲ Ornithine molecule
- Citrulline molecule

- △ Precursor molecule that converts to ornithine
- ▢ Minimal media

Bubbles indicate that *Neurospora* is growing



HERSHEY AND CHASE: DNA IS THE GENETIC MATERIAL IN VIRUSES

In the early 1950s, Alfred Hershey (born 1908) and Martha Chase (born 1927) proved that the DNA (deoxyribonucleic acid) of bacteriophages (viruses that infect bacteria) is the gene-carrying component of these organisms. They experimented with a bacteriophage called T2 and used radioactive labels to determine whether the phage DNA or protein was responsible for directing the production of new T2 phages during the infection of a bacterium.

THE EXPERIMENT

1 T2 phages (a) were grown in *E. coli* bacteria (b) with either ^{32}P to radioactively label the phage DNA (c) or with ^{35}S to radioactively label the phage protein coat (d).

2 The labeled phages were then used to infect *E. coli* grown in unlabeled media (e).

3 These bacteria became radioactively labeled when infected by DNA-labeled phages, but did not when infected by the protein-labeled phages.

Furthermore, the "ghosts" (viral coats left outside bacteria after infection) (f) of the protein-labeled T2 kept their radioactive label, while those of the DNA-labeled T2 did not.

4 The infected bacteria were able to produce progeny (new) phages (g).

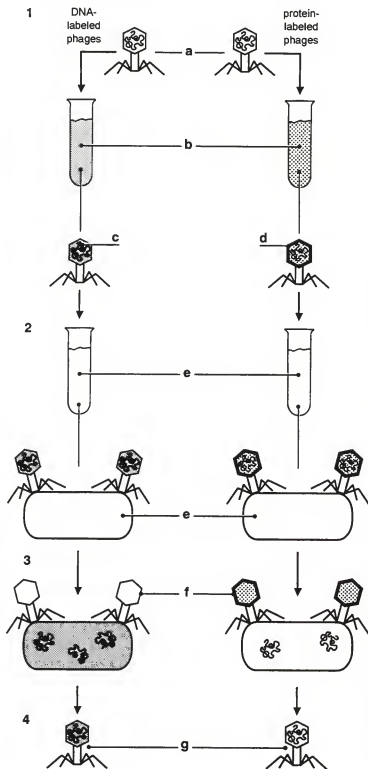
CONCLUSION

In conclusion, Hershey and Chase were able to show that DNA, and not protein, was the genetic material with which the T2 phages had infected the bacteria, thus allowing them to produce more viruses.

Key:

 ^{32}P label

 ^{35}S label

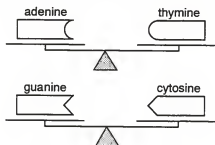


FRANCIS CRICK, JAMES WATSON, AND THE STRUCTURE OF DNA

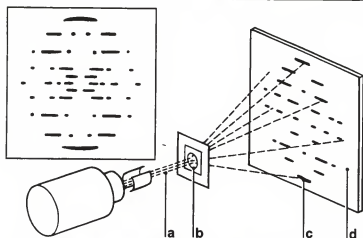
Despite previous breakthroughs, it was not until 1953 that the era of molecular genetics really began. In that year, James Watson (born 1928) and Francis Crick (born 1916) proposed a double-helix model for the structure of DNA (deoxyribonucleic acid). This model resembles a spiral ladder. Although it was based to a great extent on speculation, the double-helix DNA model has since been proven to be remarkably accurate. They used evidence such as the chemical components of DNA, the work of Erwin Chargaff (born 1905), and the work of Maurice Wilkins (born 1916) and Rosalind Franklin (1920–58) to arrive at the double-helix model.

PAIRED CHEMICALS IN DNA

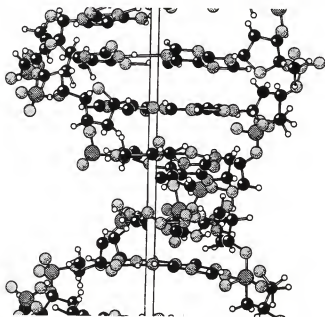
Chargaff had already separated and measured the four nucleic acid bases in DNA. He had found that the amount of adenine equals the amount of thymine, and the amount of cytosine equals the amount of guanine. This evidence led to the assumption that adenine always pairs with thymine, and guanine always pairs with cytosine.

**SHAPE OF THE DNA MOLECULE**

Wilkins and Franklin fired X rays (a) through DNA crystals (b). The X-ray beam was diffracted (scattered) by the DNA crystals. The position of spots (c) caused by the X rays on a photographic plate (d) led them to conclude that DNA molecules are helical (coiled).

**DNA MODELS**

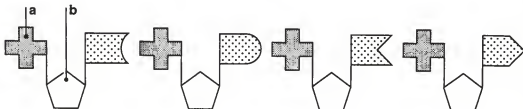
Using this information, Watson and Crick built metal models to see if they could work out what the structure of DNA might be.



DNA STRUCTURE 1: NUCLEOTIDES AND BASE PAIRING

NUCLEOTIDES

DNA (deoxyribonucleic acid) is built up from four nucleotides (building blocks) that differ only in their nitrogen bases. Each comprises a phosphate group (a), a sugar molecule (deoxyribose) (b), and one of the four nitrogenous bases: adenine, thymine, guanine, or cytosine. The full name of DNA nucleotides is deoxyribonucleotides (or deoxynucleotides).



Key to bases:

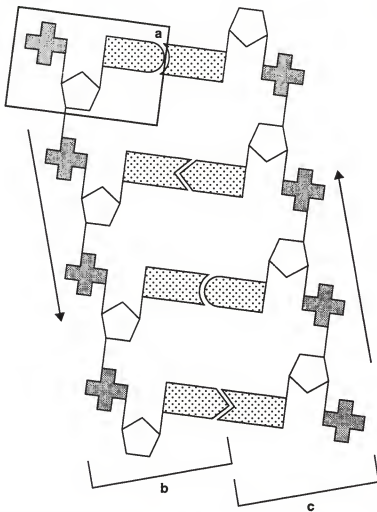


BASE PAIRING

A DNA molecule consists of many nucleotides (a) joined head-to-tail to form a long strand. Two such strands (b and c), running in opposite directions, stick together because of base pairing:

- adenine in one strand forms hydrogen bonds with thymine in the other strand, and
- guanine in one strand forms hydrogen bonds with cytosine in the other strand.

As the two DNA strands of a double helix form base pairs all the way along their length, they are said to be complementary to each other.



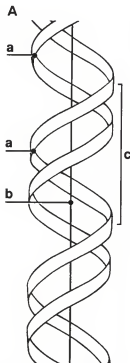
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DNA STRUCTURE 2: THE DOUBLE HELIX

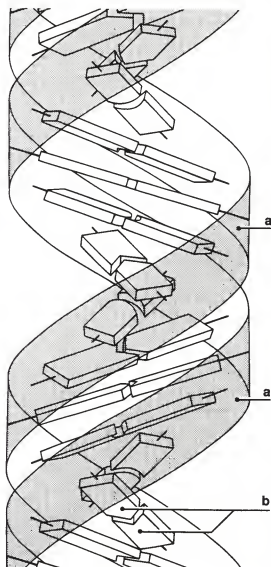
In all organisms except certain viruses, the genetic material – DNA – appears as a double-helix molecule, resembling a spiral ladder.

A SIDE VIEW

- DNA strands (a) do not twist around each other, but instead wrap around a common axis (b), like the two edges of a strip of paper wrapped around a tube.
- One complete turn (c) of each strand covers 3.4 nm.

**B DETAILED VIEW**

- The sugar-phosphate backbone of each DNA strand forms the "sides" of the ladder (a) and the base pairs form the "rungs" (b).
- The hydrogen bonds of the paired bases hold the two sides of the ladder together.

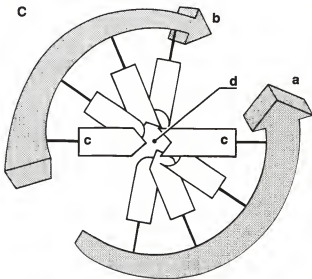


Key to bases:

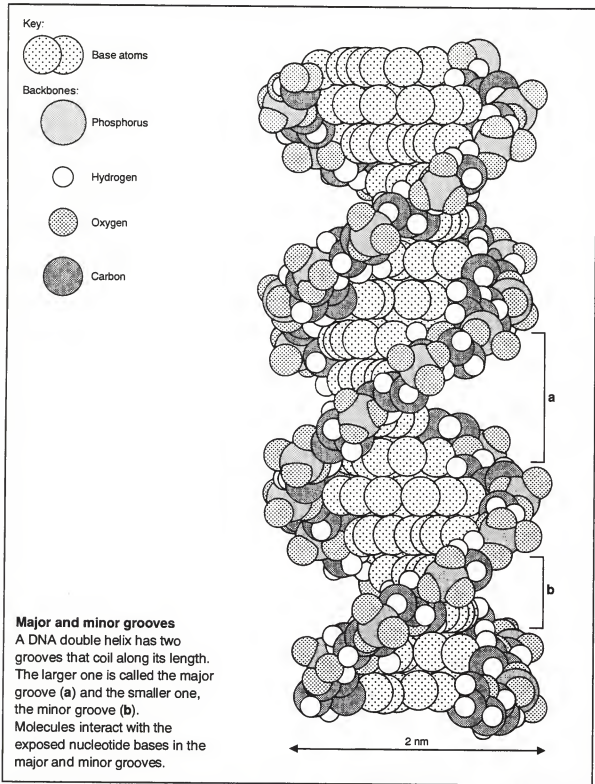
Adenine		Thymine
Guanine		Cytosine

C VIEW FROM ABOVE

- One DNA strand (a) rotates counterclockwise and its nucleotides are arranged in a sequence that "reads" upward.
- The other strand (b) rotates clockwise and its nucleotides are arranged in a sequence that "reads" downward.
- The base pairs (c) that hold the two DNA strands together are at right angles to the helix axis (d).
- There are ten base pairs for each complete turn of the helix.

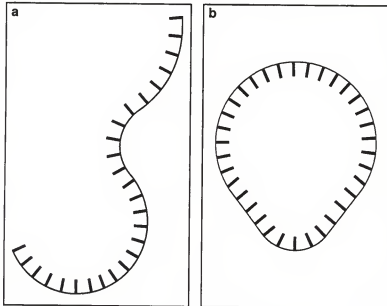


DNA STRUCTURE 3: MOLECULAR DOUBLE-HELIX MODEL



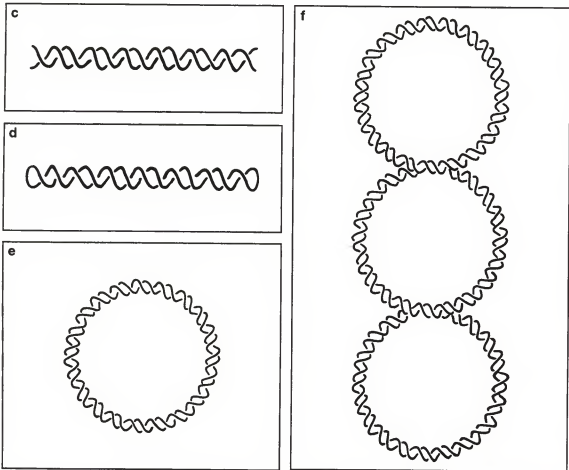
DNA STRUCTURE 4: SINGLE- AND DOUBLE-STRANDED DNA**SINGLE-STRANDED DNA**

Single-stranded DNA (deoxyribonucleic acid) (a) is usually found in viruses. A molecule of single-stranded, circular DNA (b) is one in which the two ends have been joined together. Single-stranded DNA molecules are usually only found in certain viruses.

**DOUBLE-STRANDED DNA**

Double-stranded DNA molecules (c through f) are found in viruses, bacteria, and eukaryotes, such as plants and animals. They sometimes have their ends joined together (d); are

circular (e); or may even be supercoiled (f). Supercoiled DNA is circular DNA that has been twisted into a "coiled coil."



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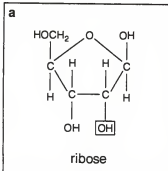
RNA STRUCTURE 1

RNA AND DNA DIFFERENCES

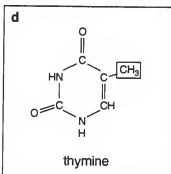
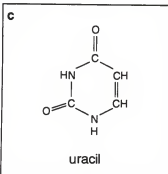
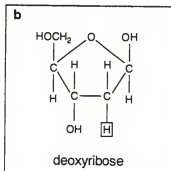
Although DNA (deoxyribonucleic acid) and RNA (ribonucleic acid) are chemically very alike, there are two important differences:

- RNA has the sugar ribose (a) instead of the sugar deoxyribose (b), which is found in DNA. These two sugars are very similar in their chemical structure.
- RNA has the nitrogenous base uracil (c), which replaces the thymine (d) found in DNA. Like thymine, uracil pairs with adenine.

RNA

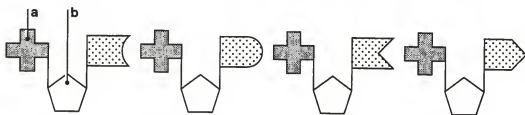


DNA



NUCLEOTIDES

RNA is made up of four nucleotides (building blocks) that differ only in their nitrogen bases. Each comprises a phosphate group (a), a ribose sugar (b), and one of the four nitrogen bases: adenine, uracil, guanine, or cytosine. The full name of RNA nucleotides is ribonucleotides.

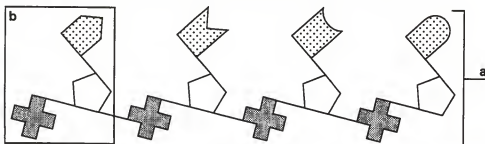


Key to bases:



RNA STRAND

An RNA strand (a) is made up from many nucleotides (b) joined head-to-tail.

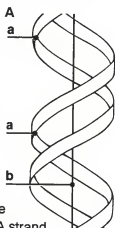


RNA STRUCTURE 2: THE DOUBLE HELIX

Although RNA generally appears as a single strand, it often forms a double-helix (spiral-ladder) shape by folding back on itself.

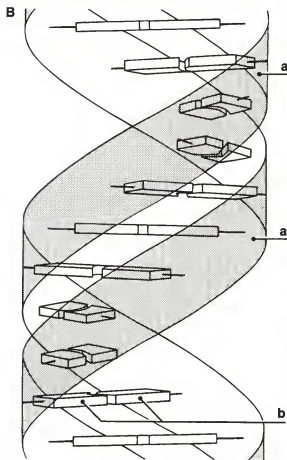
A SIDE VIEW

An RNA strand (a) does not twist around itself, but instead wraps around a common axis (b), like a strip of paper wrapped around a tube.

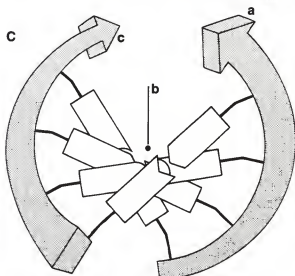
**B DETAILED VIEW**

- The sugar-phosphate backbone of the RNA strand forms the "sides" of the ladder (a) and the base pairs form the "rungs" (b).
- The hydrogen bonds between the paired bases hold the two sides of the ladder together.

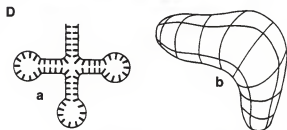
Key to bases:

**C VIEW FROM ABOVE**

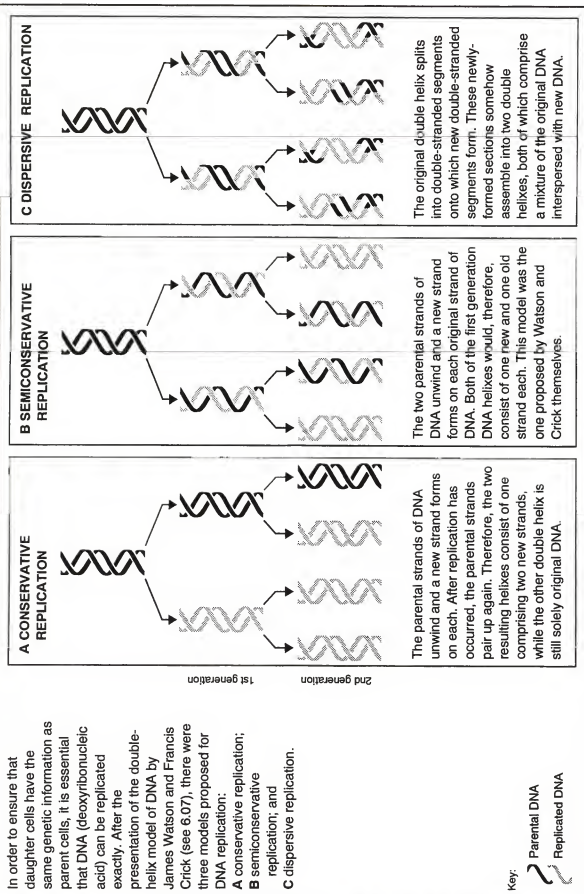
- One RNA strand (a) rotates counterclockwise around the axis (b), and its nucleotides are arranged in a sequence that "reads" upward.
- The other strand (c) rotates clockwise and its nucleotides are arranged in a sequence that "reads" downward.
- Unlike in DNA, there is a hole down the middle of an RNA double helix. This is accounted for by the small difference in structure between the RNA sugar, ribose, and the DNA sugar, deoxyribose.

**D FOLDED RNA**

- Many RNA molecules – like this tRNA (transfer RNA) molecule (a) – form double helixes by folding back on themselves rather than by pairing with a separate, complementary RNA molecule.
- The overall three-dimensional shape of the tRNA molecule (b) is like a curved bean.



DNA REPLICATION 1: THREE MODELS



DNA REPLICATION 2: MESELSON-STAHN EXPERIMENT

In 1958, Matthew Meselson (born 1930) and Franklin Stahl (born 1929) grew *E. coli* bacteria in media containing, initially, the nitrogen source ^{15}N and, subsequently, ^{14}N – both of which the bacteria incorporated into their DNA. After purification, the density of the DNA was analyzed using high-speed centrifugation. As ^{15}N DNA is more dense than ^{14}N DNA, it sinks farther down centrifuge tubes. It was possible, therefore, to trace the original DNA and the replicated DNA through the generations by comparing densities. The results were compared with those predicted by the three models of DNA replication to see which model was correct.

1 Parental (^{15}N) DNA

E. coli (a) were grown in media containing ^{15}N . The band (b) on the centrifuge tube is the heavy, ^{15}N DNA.

**2 First generation DNA**

The next *E. coli* generation (c) was grown with ^{14}N . One band (d) appeared on the centrifuge tube halfway between the levels at which ^{15}N DNA and ^{14}N DNA would settle. This DNA, therefore, comprised equal proportions of parental DNA and new, ^{14}N DNA. This ruled out the conservative model, which could not produce DNA of intermediate density.

**3 Second generation DNA**

The second *E. coli* generation (e) was also grown in ^{14}N . Two equal bands appeared on the centrifuge tube: the intermediate-level band (f) comprised DNA of equal proportions of new and original DNA, while the higher band (g) comprised only the less dense ^{14}N DNA. This result ruled out the dispersive model, but fitted the semiconservative model.



Key:
 ^{15}N medium
 ^{14}N medium

DENSITY
 low (L)
 intermediate (I)
 high (H)

This table gives the expected results for each of the three models of DNA replication.

	CONSERVATIVE	SEMICONSERVATIVE	DISPERSIVE	Parental DNA Replicated DNA
First generation (step 2)				
Second generation (step 3)				

DNA REPLICATION 3: SEMICONSERVATIVE REPLICATION

- 1 The DNA double helix (a) uncoils and the two strands (b) separate. These act as templates ("molds") for new strands.
- 2 In the presence of the enzyme (biological catalyst) DNA polymerase, free nucleotides (DNA building blocks) (c) attach to exposed complementary bases on the original strands. Adenine (A) always attaches to thymine (T), and guanine (G) always attaches to cytosine (C).
- 3 DNA polymerase then joins these free nucleotides, one at a time, onto the end of


the DNA strand that is being synthesized. The DNA polymerase then moves on to the next nucleotide of the template DNA strand, allows a complementary nucleotide to base pair with it and then joins that onto the new DNA strand. This process is repeated all the way along both of the original DNA strands.

- 4 The end result is two DNA molecules identical to the original double helix. Each consists of one new and one old strand of series of nucleotides.

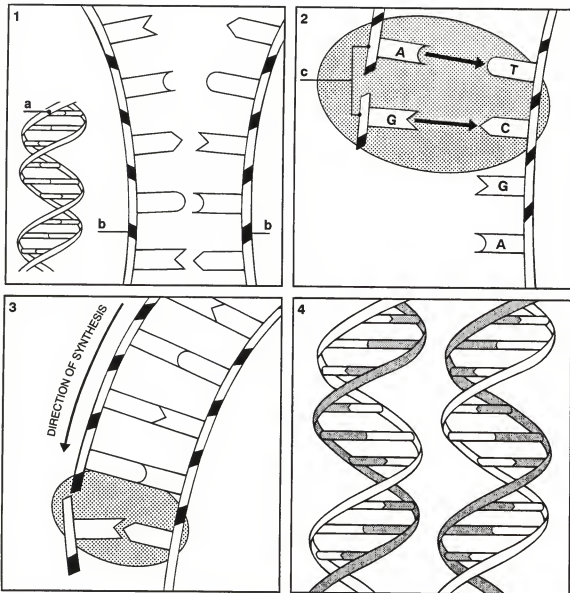
Key: Adenine  Thymine
Guanine  Cytosine

 Phosphate group

 DNA polymerase

 Sugar (deoxyribose)

 New DNA strand in final helix

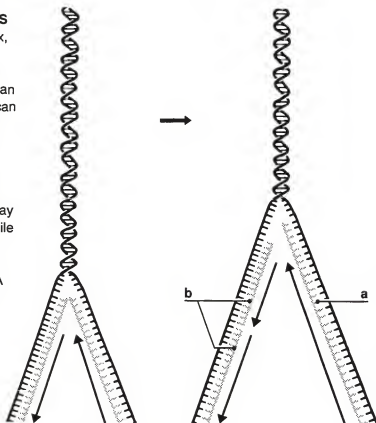


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DNA REPLICATION 4

CONTINUOUS AND DISCONTINUOUS SYNTHESIS

To replicate a DNA double helix, both DNA strands must be uncoiled and separated before the enzyme DNA polymerase can copy them. New DNA strands can be synthesized in one direction only. As the two strands in the original double helix run in opposite directions, this means that only one new DNA strand can be made in a continuous way (a) by the DNA polymerase, while the other new strand has to be made discontinuously in short segments (b). These short DNA segments are then joined together to form a new strand.



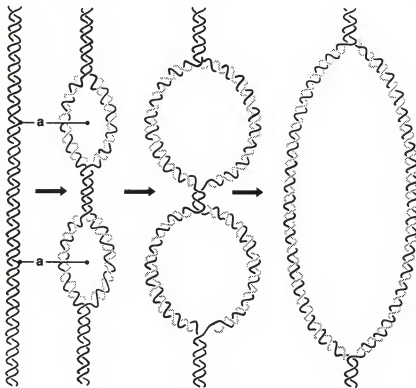
Key:

TTTT Original DNA

TTTT Replicated DNA

MULTIPLE ORIGINS

In eukaryotes, such as plants and animals, long molecules of DNA have many origins (starting points) (a) of replication. The new DNA strands eventually meet each other and join up.



Key:

Original DNA

Replicated DNA

PROTEIN SYNTHESIS 1: THE CENTRAL DOGMA**THE IMPORTANCE OF PROTEIN SYNTHESIS**

DNA (deoxyribonucleic acid) functions primarily by directing the production of proteins. Each DNA molecule can carry thousands of genes. Every gene carries the plan for building a particular protein, or part of a particular protein. As which proteins are produced decides everything about an organism from whether it is a dog or a flower to the size of leaf or fur color, this information is sometimes referred to as an organism's genetic blueprint.

THE CENTRAL DOGMA

The "Central Dogma" is a name coined, in 1956, by Francis Crick (born 1916) to describe the flow of genetic information from DNA to protein: DNA makes ribonucleic acid (RNA) makes protein. This involves two main stages: transcription and translation.

1 Transcription

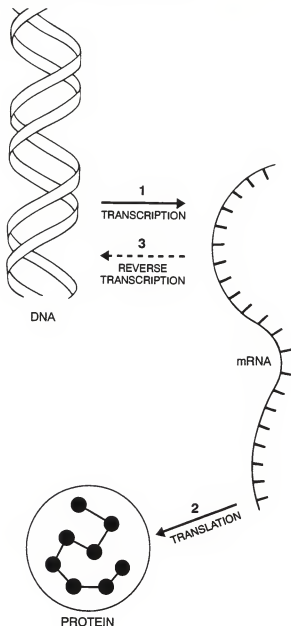
The genetic information carried by DNA – its nucleotide (building block) sequence – is transcribed (transferred) into an mRNA (messenger RNA).

2 Translation

The information in the mRNA (its nucleotide sequence) is then translated into the amino acid (building block) sequence of a protein.

3 REVERSE TRANSCRIPTION

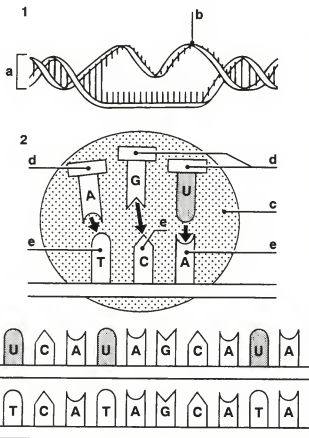
An enzyme (biological catalyst) called reverse transcriptase can make DNA by copying RNA, but there are no enzymes that can convert protein sequences into DNA or RNA sequences, and no enzymes that can make proteins directly from DNA.



PROTEIN SYNTHESIS 2: TRANSCRIPTION

The process of making RNA from DNA is called transcription.

- 1 The DNA (a) partly unwinds to make genes (sequences of bases) available for transcription. One of its strands (b) will serve as a template ("mold") to produce the RNA strand.
- 2 The enzyme RNA polymerase (c) binds to the DNA and moves along it, attaching free nucleotides (d) to the exposed complementary DNA bases (e), making a strand of RNA.
- 3 The new RNA molecule (f) has the same sequence as one of the DNA strands (g) – the one that was not the template – except that it has the base uracil instead of thymine.



Key:

Base on
DNA strand

☐ A adenine

☐ T thymine

☐ G guanine

☐ C cytosine

Complementary base
on RNA strand

☐ U uracil

☐ A adenine

☐ C cytosine

☐ G guanine

RNAs PRODUCED BY TRANSCRIPTION

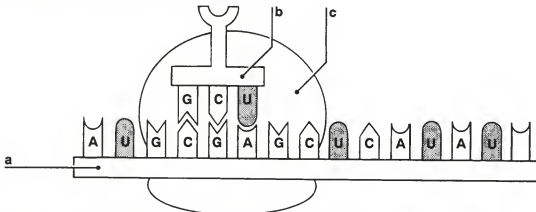
There are three types of RNA that are found in both eukaryotes, such as plants and animals, and prokaryotes (bacteria):

- mRNA (messenger RNA) (a) carries a copy of the DNA's protein-synthesis plan.
- tRNA (transfer RNA) (b) translates the protein-synthesis information on the mRNA.
- Along with certain proteins, rRNA (ribosomal RNA) forms ribosomes (tiny, granular miniorgans) (c), which help the tRNA and

mRNA to produce proteins.

- A fourth type of RNA, snRNA (small nuclear RNA) (*not shown*) is only present in eukaryotic cells. This version of RNA is involved in RNA processing events.

In prokaryotes, only one type of RNA polymerase is involved in transcribing the different RNAs. In eukaryotes, three different types of RNA polymerase are involved.

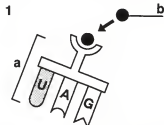


PROTEIN SYNTHESIS 3: TRANSLATION

Converting an mRNA's nucleotide sequence into a protein sequence is called translation.

BEFORE TRANSLATION

- 1 Specific tRNAs (transfer RNAs) (a) attach to particular amino acids (b). A tRNA molecule with an amino acid attached is called an aminoacyl-tRNA.

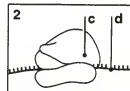
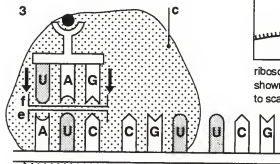


Key to bases:

Adenine	A	U	Uracil
Guanine	G	C	Cytosine

TRANSLATION**Initiation**

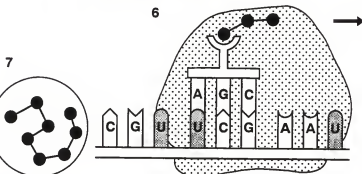
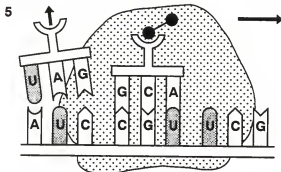
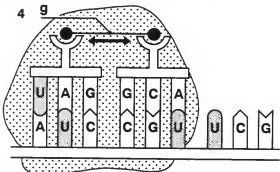
- 2 A ribosome (c) binds to an mRNA strand (d).
3 An mRNA codon (group of three bases) (e) on the ribosome (c) binds to an aminoacyl-tRNA with the appropriate complementary bases – the anticodon (f). The ribosome holds the tRNA and mRNA together.



ribosome and mRNA shown approximately to scale

Elongation

- 4 A second aminoacyl-tRNA binds to the mRNA and the ribosome. This brings the amino acid that it is carrying into contact with the one on the neighboring tRNA. The ribosome links the amino acids with a peptide bond (g).
5 The ribosome then moves along the mRNA. The first tRNA loses its amino acid – which is now attached to the second tRNA – and leaves the ribosome.
6 The cycle (steps 3–5) is repeated. As the ribosome moves along the mRNA, the chain of amino acids grows longer.
7 The finished protein has a sequence of amino acids that has been determined by the mRNA base sequence.



CRACKING THE GENETIC CODE

The genetic code is the set of rules that determines which proteins are produced by particular base sequences on mRNA (messenger RNA). Marshall Nirenburg (born 1927) and Heinrich Matthaei (born 1929) made the first steps in cracking the genetic code in 1961. This work was continued by Gobind Khorana (born 1922) in the 1960s. Nirenburg's experiments showed that three bases (a codon) in a particular order determine which amino acid (protein building block) is produced. This is called the triplet code. By tracing the amino acids synthesized from RNA molecules of known sequence, some of the genetic code could, therefore, be worked out.

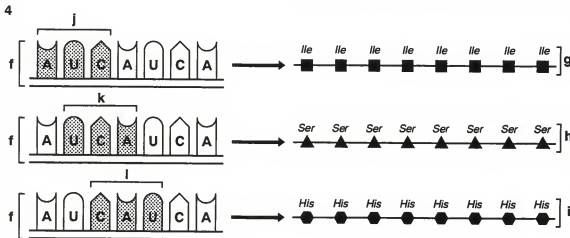
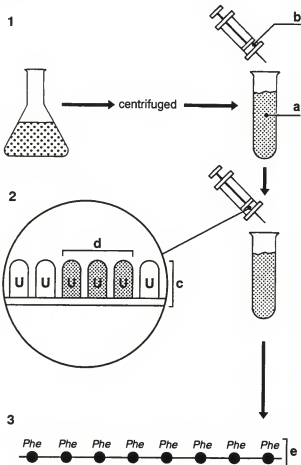
1 Nirenburg and Matthaei formulated a cell-free, protein-synthesizing mixture from centrifuged *E. coli* bacteria cells (a). Amino acids (b) were added to this mixture.

2 Chemically-synthesized RNA (c) consisting of only the base uracil (U) was added to this medium. The only possible codon was UUU (d).

3 They found that the protein produced was polyphenylalanine (e) – a chain of phenylalanine amino acids. The mRNA triplet code for phenylalanine, therefore, had to be UUU.

4 They repeated the experiment and other codons were cracked. Poly(AUC) mRNA (f), for example, made three proteins: g polyisoleucine; h polyserine; or i polyhistidine.

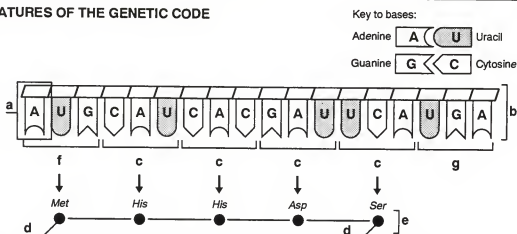
This is because poly(AUC) mRNA can be read as a sequence of either AUC (j), UCA (k), or CAU (l) codons, depending on where the translation begins.



Key to bases: Adenine A Uracil U Guanine G Cytosine C

THE GENETIC CODE

FEATURES OF THE GENETIC CODE



- The nucleotides (RNA building blocks) (a) of mRNA (messenger ribonucleic acid) (b) are read in groups of three called codons (c).
- Each codon specifies a particular amino acid (d). This is called the triplet code. Amino acids are the building blocks of proteins (e). As there are twenty amino acids coded for by RNA and sixty-four possible codons, there is more than one codon for each amino acid.
- The codons are read separately and continuously – they do not overlap and there are no gaps between them.
- AUG, which codes for methionine, acts as an initiation ("start") codon (f).
- Three particular codons (UAA, UAG, and UGA) do not specify amino acids, but act as "stop" codons (g).
- The genetic code is almost universal. In most organisms, the same codons specify the same amino acids.

THE CODONS OF THE GENETIC CODE

To find out which amino acid is added to a protein for each particular mRNA codon, see the table below.

Key:

A Adenine G Guanine
U Uracil C Cytosine

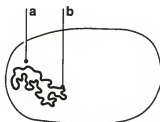
* Start codon

		second nucleotide					
		U	C	A	G		
first nucleotide	U	UUU } Phenylalanine UUC } UUA } UUG } Leucine	UCU } UCC } Serine UCA } UCG }	UAU } Tyrosine UAC } UAA } STOP UAG } STOP	UGU } Cysteine UGC } UGA } STOP UGG } Tryptophan	U	
	C	CUU } CUC } Leucine CUA } CUG }	CCU } CCC } Proline CCA } CCG }	CAU } Histidine CAC } CAA } Glutamine CAG }	CGU } Arginine CGC } CGA } CGG }	C	
	A	AUU } AUC } Isoleucine AUA } AUG* } Methionine	ACU } ACC } Threonine ACA } ACG }	AAU } Asparagine AAC } AAA } Lysine AAG }	AGU } Serine AGC } AGA } Arginine AGG }	A	
	G	GUU } GUC } Valine GUA } GUG }	GCU } GCC } Alanine GCA } GCG }	GAU } Aspartic acid GAC } GAA } Glutamic acid GAG }	GGU } GGC } Glycine GGA } GGG }	G	

If U was replaced with A; A replaced with T and vice versa; and G replaced with C and vice versa; the table would show how the DNA (deoxyribonucleic acid) sequence of a gene is related to the amino acid sequence of a protein.

BACTERIAL GENETICS 1: BACTERIAL CHROMOSOMES AND PLASMIDS**BACTERIAL CHROMOSOMES**

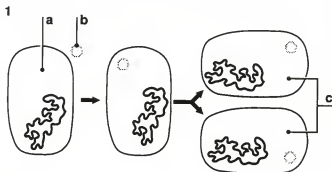
The genes of a bacterium (a) are normally located on a single, circular chromosome composed of one DNA (deoxyribonucleic acid) molecule (b).

**PLASMIDS**

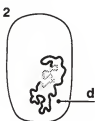
Plasmids are small, circular molecules of DNA that can exist inside bacterial cells.

1 Transformation

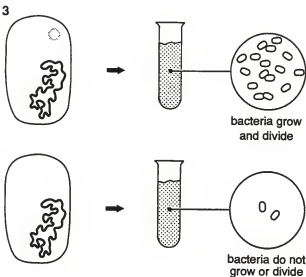
A bacterium (a) can often take up a plasmid (b) from its surroundings – this is called transformation. Any plasmids will be transferred to both daughter cells (c) when a bacterium divides into two new cells.

**2 Integration**



Sometimes, plasmids become inserted into the bacterial chromosome (d). This is called integration.

**3 Effects of plasmids**

A plasmid may carry genes that a bacterium does not normally need to grow and survive, but which can offer the bacterium useful additional properties, such as being able to break down antibiotics (as in the case of genes that confer resistance to antibiotics).



Key:

-  Plasmid carrying genes that confer resistance to antibiotics
-  Medium containing antibiotics

BACTERIAL GENETICS 2: OVERVIEW OF DNA TRANSFERS

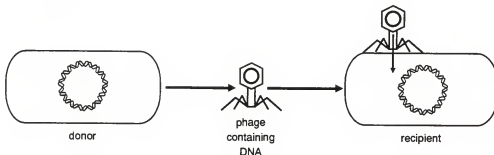
Bacteria can acquire DNA from other bacteria in a variety of ways. This enables them to gain new abilities (virulence or resistance to antibiotics, for example) and promotes genetic variability in a way that reproduction by binary fission (simple division) does not allow.

TRANSFORMATION



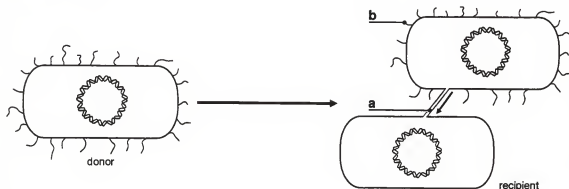
A free, naked DNA molecule can be transferred from a donor to a recipient bacterium or picked up from the environment. This may happen when the donor's cell (plasma) membrane is ruptured and the genome (complete set of genes) escapes. In this way, living bacteria can even pick up genes from dead bacteria.

TRANSDUCTION



DNA can also be transferred by a bacteriophage (phage) – a virus that infects bacteria. A phage can carry a portion of the DNA from one bacterium to another. The DNA sequence may be destroyed by enzymes (biological catalysts) or it may be combined into the host's genome.

CONJUGATION

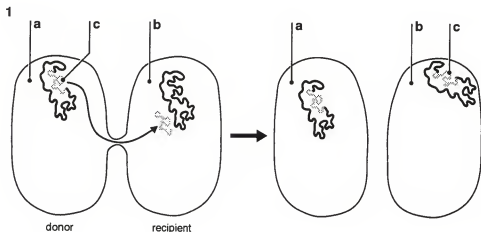


This process has been likened to sexual reproduction. It involves direct contact between two bacteria. The bacteria become linked by a hypha (a), which is formed by the extension of a pilus (cell membrane projection) (b). This acts as a bridge for the transfer of DNA.

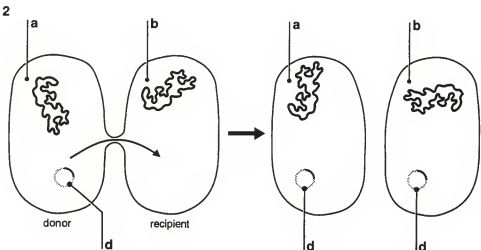
BACTERIAL GENETICS 3: CONJUGATION

In some cases a bacterium can donate a copy of some or all of its DNA to another bacterium. This is called conjugation.

- 1 One bacterium (a) is the DNA donor and the bacterium (b) that receives the DNA (c) is the recipient. In this way, antibiotic resistance can spread between different bacterial strains. If the genes required for conjugation are on the donor bacterium's chromosome, then the recipient bacterium can receive a copy of some or all of the donor's chromosomal DNA. The genes responsible for conjugation are always the last genes to be transferred and conjugation often ends before this happens.



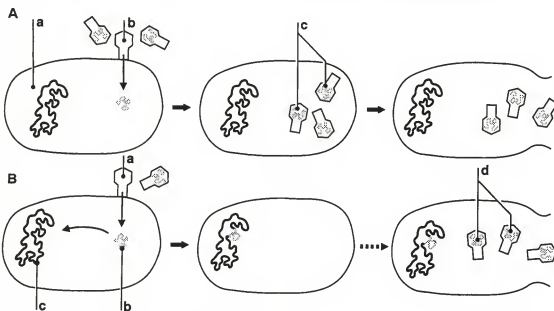
- 2 If the genes that allow conjugation to occur are on a plasmid (d), only a copy of the plasmid may be transferred from donor to recipient.



BACTERIAL GENETICS 4: IMPACTS OF VIRAL INFECTION

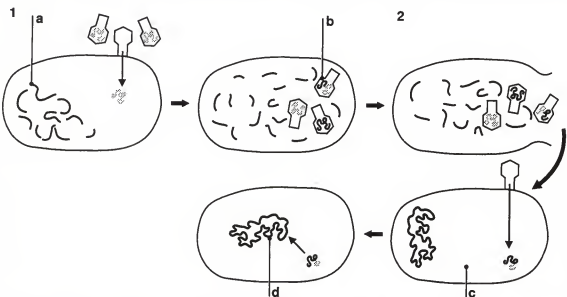
A LYTIC GROWTH

After infecting a bacterial cell (a) a virus (b) may immediately start to produce progeny (new) viruses (c) that are released from the host cell. This is called lytic growth and results in the death of the bacterium soon after infection.

**TRANSDUCTION**

- 1 If the host's chromosome (a) breaks up during the infection, a few viruses (b) are formed that contain some host DNA as well as the viral DNA.
- 2 These viruses can introduce this DNA into their new host (c), and the introduced DNA can become integrated in the new host's chromosome (d).

The whole process of disintegration, transfer, and integration of host DNA is called transduction.

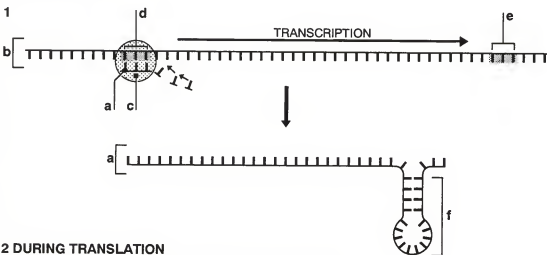


GENE EXPRESSION IN PROKARYOTES 1

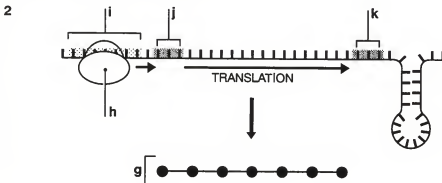
Prokaryotes (bacteria) do not live in unchanging environments; so they need to be able to compensate for environmental changes. One way of achieving this is to regulate the expression of genes so that only products appropriate to the current conditions are made. There are various regulatory mechanisms that make sure only necessary genes are expressed (transcribed and translated). These can involve, for example, the use of certain enzymes (biological catalysts), "promoters," and proteins that serve to switch genes "on" or "off."

1 DURING TRANSCRIPTION

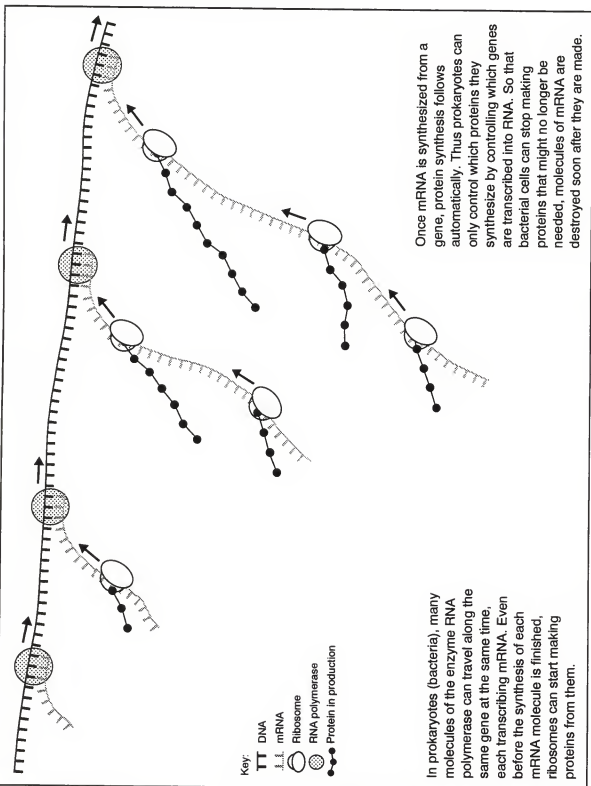
The process of making mRNA (messenger ribonucleic acid) (a) from DNA (deoxyribonucleic acid) (b) is called transcription. An enzyme called RNA polymerase (c) binds to a short region of a gene on the DNA called a promoter (d). It then moves along the DNA, synthesizing mRNA, until it passes a "stop" sequence (e). The mRNA synthesized at the stop sequence folds into a loop (f) and, in effect, pushes the RNA polymerase off the DNA.

**2 DURING TRANSLATION**

Converting mRNA's genetic information into a protein (g) is called translation. A ribosome (granular miniorgan) (h) binds to the mRNA at a sequence called the ribosome-binding site (i). The ribosome moves along the mRNA until it finds a start codon (the base sequence AUG) (j). The ribosome then synthesizes protein until it passes a stop codon (k) – three bases that do not specify an amino acid (protein building block) .



GENE EXPRESSION IN PROKARYOTES 2



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JACQUES MONOD, FRANCIS JACOB, AND BACTERIAL OPERONS 1

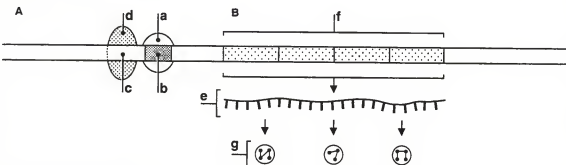
In 1961, Jacques Monod (1910–76) and Francis Jacob (born 1920) published their findings on how bacteria control which genes they express. They described two important mechanisms:

A Activator and repressor proteins

These proteins (a) bind to operator sequences (b) near to a gene's promoter (c). They either help or prevent the enzyme (biological catalyst) RNA polymerase (d) from transcribing mRNA (messenger RNA) (e). This effectively switches genes "on" or "off."

B Operons

Some bacterial genes (f) that code for proteins which function together are both grouped together and controlled together. These clusters of genes are called operons. Operons produce polycistronic mRNA molecules (e) – which encode for more than one protein (g) – so their products are also expressed (transcribed and translated) together.

**THE *lac* OPERON**

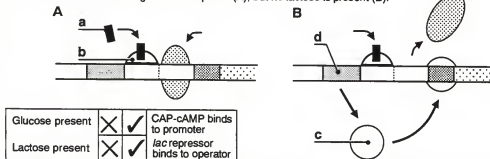
Monod and Jacob studied a particular operon called the *lac* operon. This codes for the three enzymes that *E. coli* bacteria need in order to use the sugar lactose as an energy source. As the products of the *lac* operon are not required all the time – *E. coli* usually use the energy source glucose – the bacteria need to be able to control the expression of these genes. This prevents them from expending energy on the production of unnecessary proteins. The control of *lac* operon expression is now largely understood. It is known to hinge on two factors: the presence of glucose and the presence of lactose.

Key:

- Structural gene
- Operator
- Promoter (dotted line indicates boundary of CAP-cAMP binding site)
- RNA polymerase
- mRNA strand
- Regulatory gene

lac operon

1 The bacterium's available glucose is depleted (A), but no lactose is present (B).



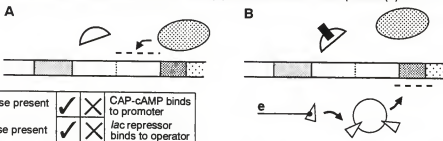
A In response to the low level of glucose, the bacterium accumulates a molecule called cyclic AMP (cAMP) (a). cAMP binds to a protein called CAP (catabolite activator protein) (b). The CAP-cAMP complex binds to the promoter in the *lac* operon. The presence of CAP-cAMP promotes the binding of RNA polymerase to the bacterial DNA (deoxyribonucleic acid).

B As there is no lactose present, a second protein called the *lac* repressor (c) is produced by the expression of the *lac* I gene (d). The *lac* repressor binds to the operator sequence of the *lac* operon. The presence of the *lac* repressor effectively "pushes" the RNA polymerase off the DNA, preventing it from transcribing the *lac* operon. Therefore, the *lac* operon is switched off.

© DIAGRAM

JACQUES MONOD, FRANCIS JACOB, AND BACTERIAL OPERONS 2

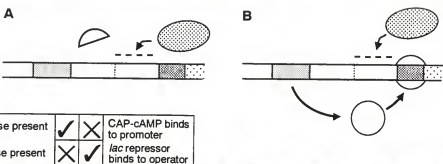
2 The bacterium's available glucose is not depleted (A) and there is also lactose present (B).



A The binding of RNA polymerase is inhibited as there is no CAP-cAMP complex bound to the promoter.

B Some of the lactose gets converted into allolactose (e), which binds to the *lac* repressor protein, preventing it from binding to the operator. This would allow the transcription of the *lac* operon genes, but only if the RNA polymerase has bound to the DNA, which has not happened in this case. Therefore, the *lac* operon is switched off.

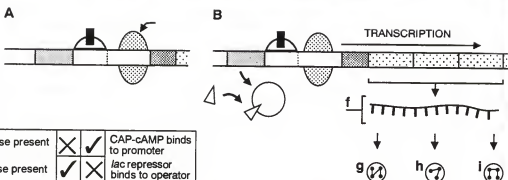
3 The bacterium's available glucose is not depleted (A) and there is no lactose present (B).



A The binding of RNA polymerase is inhibited as there is no CAP-cAMP complex bound to the promoter.

B The inducer allolactose is not produced as there is no lactose present; so the *lac* repressor is able to bind to the operator. This prevents transcription of the *lac* operon. Therefore, the *lac* operon is switched off.

4 The bacterium's available glucose is depleted (A) and there is lactose present (B).



A The binding of RNA polymerase is promoted as there is a CAP-cAMP complex bound to the promoter.

B The inducer allolactose is produced; so *lac* repressor is unable to bind to the operator. Therefore, the *lac* operon is switched on. RNA polymerase transcribes the DNA, producing a polycistronic mRNA strand (f). The mRNA is translated and the enzymes β -galactosidase (g); galactoside permease (h); and galactoside transacetylase (i) are produced. These enable the bacterium to start using the lactose as an energy source.

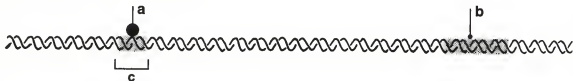
SUMMARY

Expression of the *lac* operon only occurs if the CAP-cAMP complex, but not the *lac* repressor, is bound to the *lac* operon. That is, the bacterium is both low in available glucose and is in the presence of lactose. CAP-cAMP is said to be a positive control as its presence is required to switch the operon on; the *lac* repressor is a negative control as its absence is required.

EUKARYOTIC GENE EXPRESSION

The expression (transcription and translation) of the genes of eukaryotes, such as plants and animals, differs from that of prokaryotic (bacterial) genes in several respects.

In eukaryotes, for example, a protein (a) that regulates the rate of transcription of a gene (b) may bind to a DNA (deoxyribonucleic acid) sequence (c) a great distance (several thousand base pairs) away from the target gene.



This is rare in prokaryotes but usual in eukaryotes. It means a eukaryotic gene plus its regulatory sequences can be some 50,000-nucleotides (DNA building blocks) long.

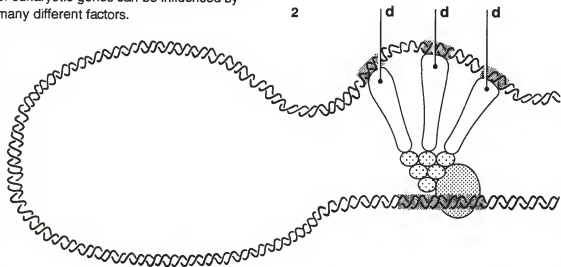
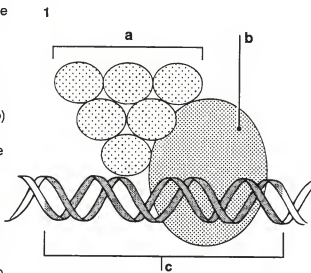
TRANSCRIPTION FACTORS

Transcription of eukaryotic genes cannot be accomplished by the enzyme (biological catalyst) RNA polymerase alone.

1 Eukaryotic transcription requires several additional proteins, called transcription factors (a). Complexes of transcription factors combine with RNA polymerase (b) at a gene's promoter (c).

2 The formation of these complexes can be either helped or hindered by regulatory proteins (d) bound to the DNA some distance away from the gene. When the DNA loops back on itself, they come into contact with the enzyme-protein complex at the gene to be transcribed.

Various regulatory proteins, each binding to different DNA sequences, can all regulate one gene. This means that the transcription of eukaryotic genes can be influenced by many different factors.



PROCESSING OF EUKARYOTIC mRNA

INSIDE THE NUCLEUS

In eukaryotes, such as plants and animals, RNA (ribonucleic acid) is processed inside the nucleus (cell control center).

1 When DNA (deoxyribonucleic acid) (a) is transcribed into RNA, the initial RNA produced is called the primary transcript (b).

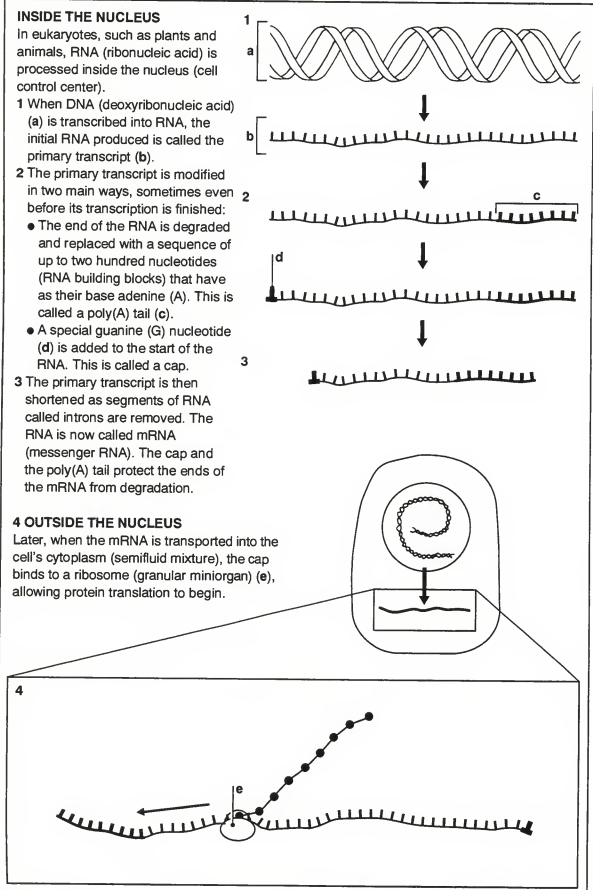
2 The primary transcript is modified in two main ways, sometimes even before its transcription is finished:

- The end of the RNA is degraded and replaced with a sequence of up to two hundred nucleotides (RNA building blocks) that have as their base adenine (A). This is called a poly(A) tail (c).
- A special guanine (G) nucleotide (d) is added to the start of the RNA. This is called a cap.

3 The primary transcript is then shortened as segments of RNA called introns are removed. The RNA is now called mRNA (messenger RNA). The cap and the poly(A) tail protect the ends of the mRNA from degradation.

4 OUTSIDE THE NUCLEUS

Later, when the mRNA is transported into the cell's cytoplasm (semifluid mixture), the cap binds to a ribosome (granular miniorgan) (e), allowing protein translation to begin.



INTRONS AND EXONS

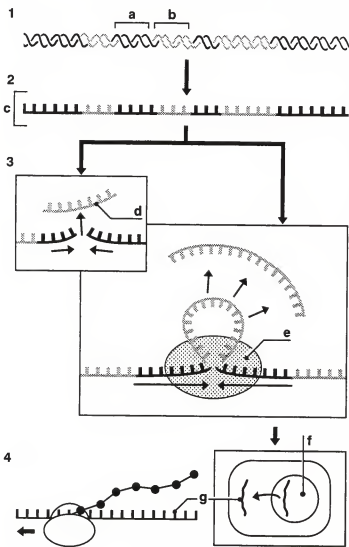
A dramatic difference between the genes of eukaryotes, such as plants and animals, and prokaryotes (bacteria) is the presence of introns and exons, which are only found in eukaryotes.

1 In eukaryotic genes, the DNA (deoxyribonucleic acid) sequence that codes for a protein can be split up into several blocks called exons (a). These are separated by DNA sequences called introns (b), which do not code for proteins.

2 The primary (initial) RNA (ribonucleic acid) transcript (c) contains both the introns and exons. The introns must be removed before the RNA passes from the nucleus (control center) into the cytoplasm (semifluid mixture) as mRNA (messenger RNA).

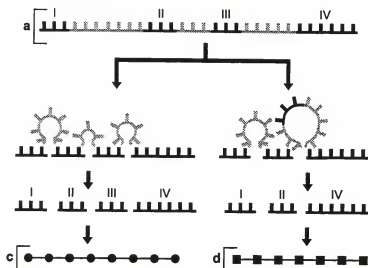
3 Some introns can actually remove themselves from a molecule of RNA, and are called self-splicing introns (d). Most, however, require complexes of protein and RNA called spliceosomes (e) to effect their removal.

4 After the introns, and perhaps some exons, have been removed, the primary RNA leaves the nucleus (f) as mRNA (g). It can then begin protein translation.



ALTERNATIVE SPLICING

Genes that contain several exons can be used to produce more than one type of protein. This is because different exons can be left out of the final mRNA molecules. This is called alternative splicing. For example, from a gene (a) with four exons (I–IV), two different proteins (c and d) might be produced, depending on which exons are left out. This, in turn, can depend on which tissue or organ the gene is expressed in.

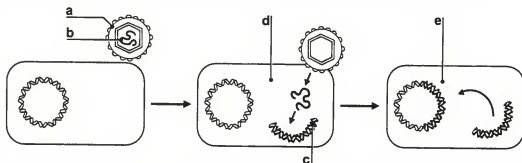


TRANSPOSABLE ELEMENTS

Transposable elements (or transposons) are mobile DNA (deoxyribonucleic acid) sequences that insert themselves into chromosomes. They can cause gene inactivations, chromosome rearrangements, and other genetic changes.

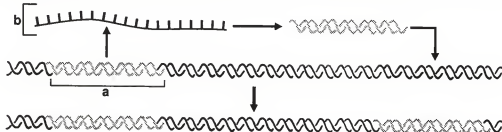
RETROVIRUSES

Retroviruses (a) are viruses that contain RNA (ribonucleic acid) (b) that is converted into DNA (c) when a host cell (d) is infected. The viral RNA codes for the enzyme (biological catalyst) reverse transcriptase, which copies the RNA into DNA. The viral RNA also codes for the enzyme integrase, which inserts the viral DNA into the host cell's chromosome (e).



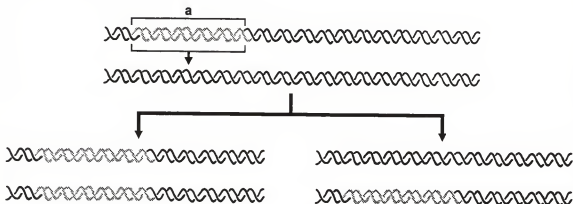
RETROTRANSPOSONS

Retrotransposons are found in most eukaryotic genomes (complete sets of genes) and behave like retroviruses that cannot form viral particles. Retrotransposon DNA (a) can be transcribed into an RNA molecule (b) that encodes for both reverse transcriptase and integrase. So, like the RNA of retroviruses, they are transposable elements that can hop around a cell's chromosomes.



OTHER TRANSPOSABLE ELEMENTS

Other types of transposable elements (a) do not need to be converted into RNA in order to move from one DNA location to another. They can move directly from one site to the next, sometimes copying themselves in the process.

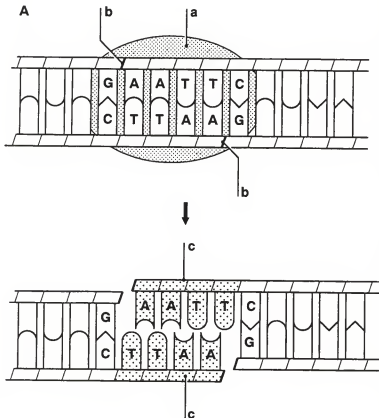


HAMILTON SMITH AND RESTRICTION ENZYMES

In 1970, the molecular biologist Hamilton Smith (born 1931) discovered an enzyme (biological catalyst) called *Hind*III. This enzyme is able to cut each of the two strands of a DNA (deoxyribonucleic acid) molecule at very specific places – where a particular nucleotide (DNA building block) sequence occurs. Since then, many more of these restriction enzymes have been found, each cutting DNA at different sites.

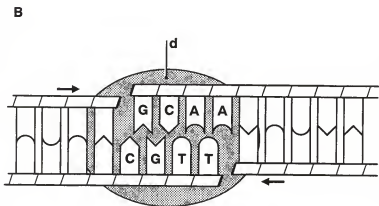
A CUTTING DNA

For example, an enzyme found in *E. coli* bacteria called *Eco*RI (a) recognizes the DNA sequence GAATTC and cuts each DNA strand after its guanine (G) nucleotide (b). This leaves two DNA molecules, each with overhanging ends (c).

**B LIGATING DNA**

An enzyme called DNA ligase (d) can ligate (join) two molecules of DNA together, especially if the DNA molecules have been cut with an enzyme like *Eco*RI that leaves overhanging ends. This is because base pairing between the overhanging ends can still hold the two DNA molecules together. For this reason, overhanging ends are also called "sticky ends."

Whenever two different DNA molecules are cut with the same restriction enzyme, even if they were from completely different organisms, they can be joined together with DNA ligase because they both have the same sticky ends.



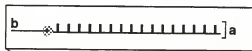
Key to bases:

Guanine  CytosineThymine  Adenine

MAXAM-GILBERT DNA SEQUENCING 1

In 1977, Allan Maxam and Walter Gilbert (born 1932) developed a method to determine the base sequence of deoxyribonucleic acid (DNA). It involved chemically "cutting up" DNA chains at specific locations. This method is known as Maxam-Gilbert DNA sequencing.

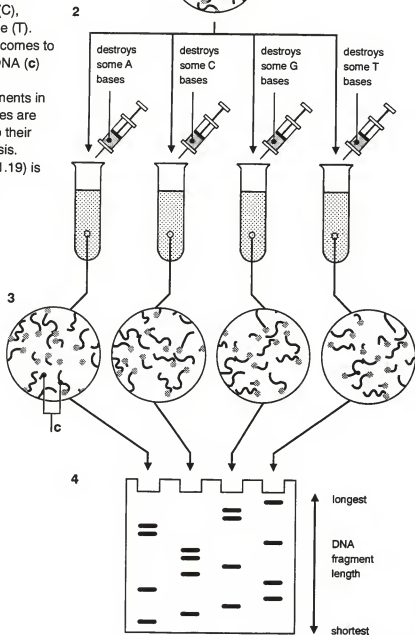
1 Double stranded DNA is labeled with ^{32}P and then separated into single strands. The "heavier" strand (a) carries the ^{32}P label at one end (b).



2 The labeled DNA sample is then divided among four tubes. Each sample is chemically treated to partially destroy one of the four bases of DNA: adenine (A), cytosine (C), guanine (G), or thymine (T).

3 As a result, each tube comes to contain fragments of DNA (c) of different lengths.

4 The labeled DNA fragments in each of the four mixtures are separated according to their length by electrophoresis. Autoradiography (see 1.19) is used to visualize the radioactive fragments.



(continued on 6.37)

MAXAM-GILBERT DNA SEQUENCING 2

5 ANALYSIS OF ELECTROPHORESIS RESULTS

The smallest DNA fragments travel farthest and are found toward the bottom of the gel. This effectively measures the fragments and the distance of the cleavage site from the labeled end of the DNA can be determined. By reading the order of the bands on the gel from the bottom – smallest DNA fragments – up (from 1 to 16), the DNA sequence can be determined.

(continued from 6.36)

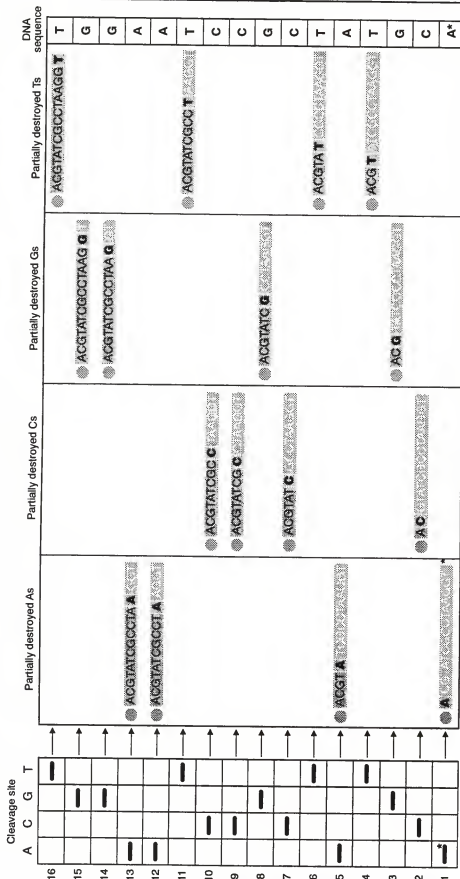
Key:

32P radioactive label

Radioactively-labeled DNA

Unlabeled DNA

Cleavage site



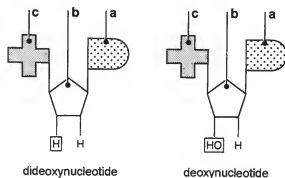
*This base is determined as only a fragment of radioactively-labeled phosphate is found.

SANGER'S DIDEOXY DNA SEQUENCING 1

In the late 1970s, Frederick Sanger (born 1918) developed a method to rapidly determine the base sequence of DNA (deoxyribonucleic acid) using the enzyme (biological catalyst) DNA polymerase. He also used dideoxynucleotides (or dideoxynucleotides), which are very similar to the deoxyribonucleotides (or deoxynucleotides) normally found in DNA.

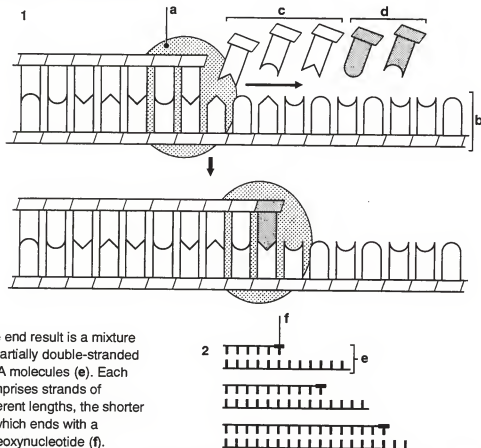
STRUCTURE OF DIDEOXYNUCLEOTIDES

Nucleotides (DNA building blocks) consist of a base (a), sugar (b), and a phosphate group (c). A dideoxynucleotide has a slightly different sugar than that of a deoxynucleotide.



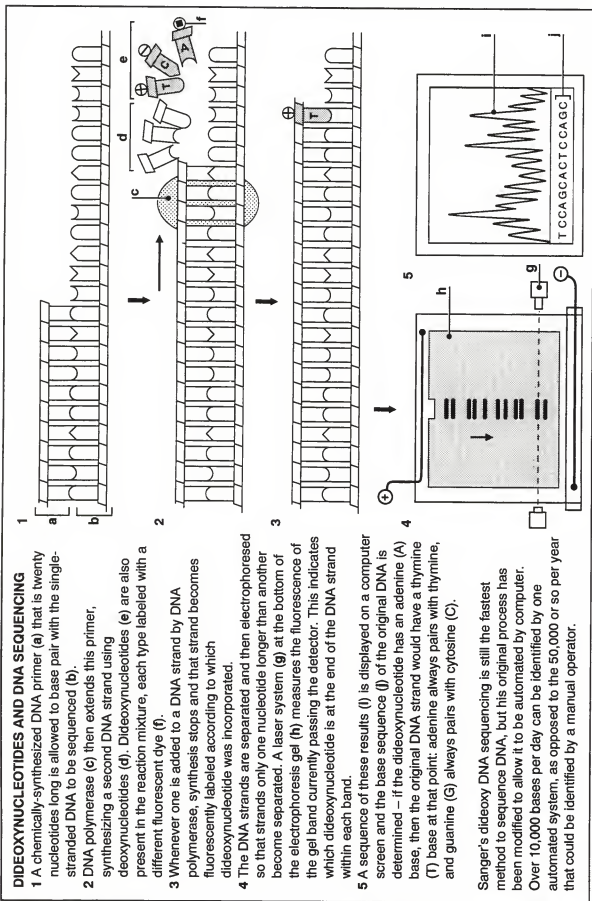
FUNCTION OF DIDEOXYNUCLEOTIDES

1 When DNA polymerase (a) copies a template strand of DNA (b) in the presence of deoxynucleotides (c) and low concentrations of dideoxynucleotides (d), the dideoxynucleotides can be added to the end of the growing DNA molecule by DNA polymerase, but no further nucleotides can then be added to them. In other words, dideoxynucleotides are chain terminators, because they prevent DNA chains from being extended by DNA polymerase.



2 The end result is a mixture of partially double-stranded DNA molecules (e). Each comprises strands of different lengths, the shorter of which ends with a dideoxynucleotide (f).

SANGER'S DIDEOXY DNA SEQUENCING 2



THE POLYMERASE CHAIN REACTION

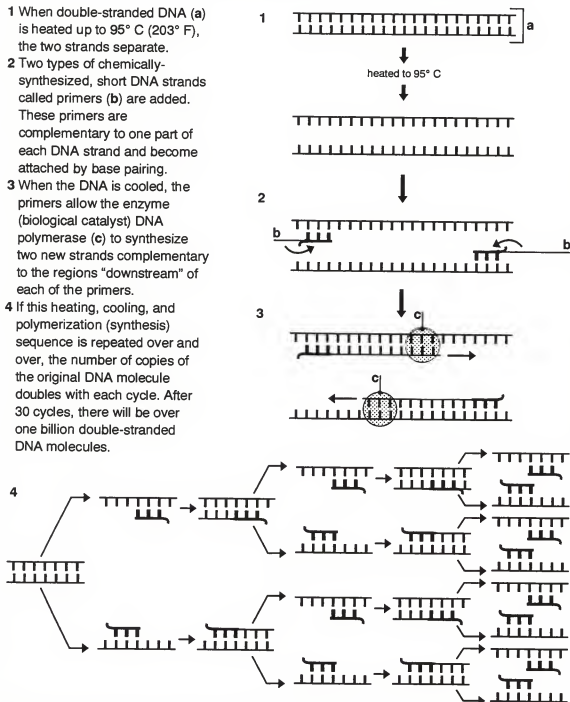
In the mid-1980s, Kary Mullis (born 1944) developed PCR (the polymerase chain reaction) as a way of copying specific DNA (deoxyribonucleic acid) molecules. This technique enables very small samples of DNA – even a single molecule – to be amplified, enabling analysis of trace amounts. PCR is used in forensic science, where it is coupled with genetic fingerprinting (see 6.49). In medicine, PCR helps to diagnose genetic disorders and low-level viral infections.

1 When double-stranded DNA (a) is heated up to 95° C (203° F), the two strands separate.

2 Two types of chemically-synthesized, short DNA strands called primers (b) are added. These primers are complementary to one part of each DNA strand and become attached by base pairing.

3 When the DNA is cooled, the primers allow the enzyme (biological catalyst) DNA polymerase (c) to synthesize two new strands complementary to the regions "downstream" of each of the primers.

4 If this heating, cooling, and polymerization (synthesis) sequence is repeated over and over, the number of copies of the original DNA molecule doubles with each cycle. After 30 cycles, there will be over one billion double-stranded DNA molecules.



Most DNA polymerases are destroyed by being heated to 95° C, but some DNA polymerases have been isolated from bacteria that live at very high temperatures. Using these polymerases means that PCR can be carried out automatically by a machine that does not have to keep adding fresh polymerase at the start of each cycle.

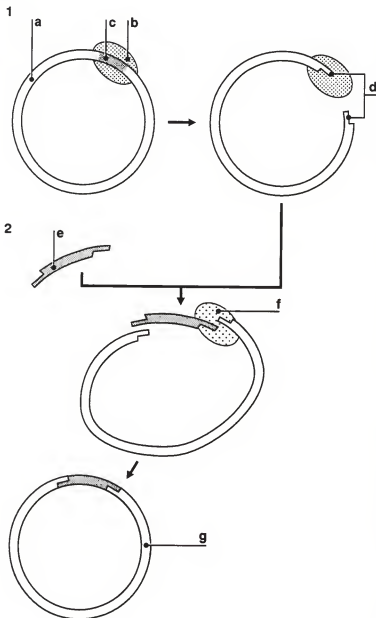
RECOMBINANT DNA

In 1972, Janet Mertz (born 1949) and Ron Davis (born 1941) noted that when the enzyme *EcoRI* produced "sticky ends" by cutting DNA (deoxyribonucleic acid), these ends could be rejoined using the enzyme DNA ligase. *EcoRI* is a type of restriction enzyme – a biological catalyst that can "cut" DNA at specific places.

In 1973, Herbert Boyer (born 1936) and Stanley Cohen (born 1935) used this information to produce the first recombinant bacterial plasmid. They joined together two different DNA molecules that had both been cut with *EcoRI*.

1 First, Boyer and Cohen cut an *E. coli* plasmid (circular DNA that is separate from the cell's own chromosome) called pSC101 (a) with *EcoRI* (b). This plasmid has a single recognition site (c) for *EcoRI*, and it was cut into a linear molecule with sticky (overhanging) ends (d).

2 Another DNA molecule was also cut with *EcoRI*. This foreign DNA (e) was then mixed with the linearized pSC101 plasmid and the molecules joined together with enzyme DNA ligase (f). The hybrid DNA molecule produced (g) was a recombinant DNA.



CLONING DNA

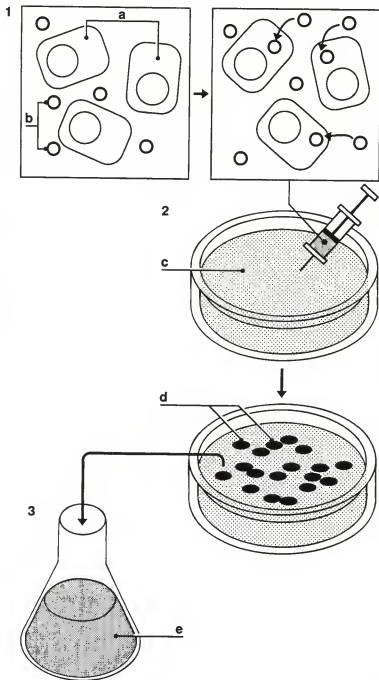
A clone is a collection of molecules, cells, or organisms that comprises identical copies of a single ancestor.

1 Bacteria (a) can be transformed with plasmids (b) carrying genes that confer resistance to an antibiotic. Some bacteria take up the plasmids, which are circular DNA (deoxyribonucleic acid) molecules separate from the bacterial chromosome. Those bacteria that do are said to have been transformed.

2 The bacteria are then able to grow on an agar plate (c) in the presence of the antibiotic. Individual colonies (d) of transformed bacteria grow. Those that did not take up the plasmid are killed by the antibiotics. Each colony is a clone of a single bacterium that had taken up a plasmid.

If the original plasmid was a recombinant molecule (containing some foreign DNA), then the foreign DNA is said to have been cloned.

3 DNA cloned in bacteria can be produced readily by simply growing more bacteria; for example, by transferring some bacteria from a single colony on an agar plate to a large liquid culture (e).



APPLICATIONS

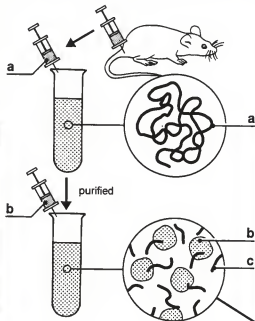
The ability to clone genes allows:

- the production of large-enough quantities of sample DNA for research and analysis;
- the production of significant quantities of the cloned gene's product (a protein such as an antibody), for profit or research; and
- the analysis of precise changes in a gene's structure and the impact on the gene's product.

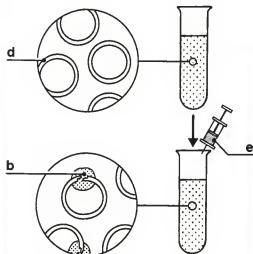
DNA LIBRARIES

A DNA (deoxyribonucleic acid) library is a collection of cloned DNA molecules that between them contain all or most of an organism's DNA. Creating a DNA library involves the use of restriction enzymes – biological catalysts that “cut” DNA at specific points – and vector (carrier) DNA molecules, which allow DNA from one organism to be propagated in another organism. For example, plasmids (circular DNA separate from a bacterium's own chromosome) and some bacterial viruses can be used as vectors for cloning foreign DNA in bacteria.

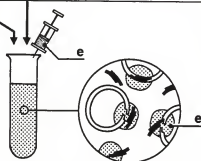
- 1 The organism's DNA (a) is first purified and then digested with a restriction enzyme (b), which cuts the DNA into fragments (c).



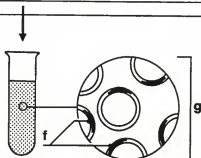
- 2 The vector DNA (d) is cut with the same enzyme (b) used to cut the foreign DNA.



- 3 The two types of DNA are then ligated (joined together) using the enzyme DNA ligase (e).



- 4 Because the vector is being ligated with a mixture of all the organism's DNA, many of the resulting recombinant vector DNA molecules (f) will contain different foreign DNA inserts. This collection of recombinant molecules is called the library (g).



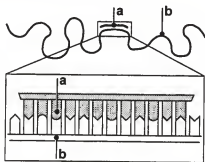
DNA PROBES AND SOUTHERN BLOTTING

A DNA probe is a single-strand length of DNA (deoxyribonucleic acid) usually of known base sequence. The essential points about probes are:

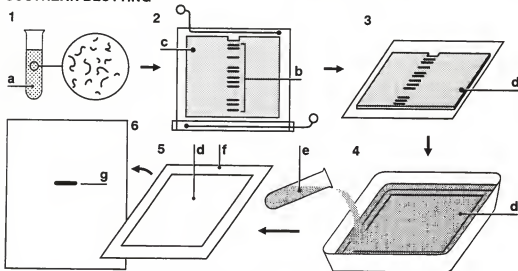
- The probe base sequence is complementary to the DNA it is used to find;
- for every guanine base to be found, the probe has a cytosine base, and vice versa; and
- for every adenine to be found, the probe has a thymine base, and vice versa.
- Probes can be radioactively or fluorescently labeled by the addition of radioactive atoms or fluorescent molecules. Any DNA such a probe anneals to (base pairs with) can then be detected using photographic film – if it is radioactive – or ultraviolet light if the label is fluorescent.
- DNA probes are used to see if a sample contains DNA complementary to the probe. This is done by Southern blotting.

HOW A PROBE WORKS

Short sequences of single-stranded DNA, 20–50-nucleotides (building blocks) long, can be chemically synthesized and then made radioactive or fluorescent. This DNA (a) can base pair with a complementary DNA or RNA (ribonucleic acid) strand (b), labeling it as either radioactive or fluorescent.



SOUTHERN BLOTTING



- 1 The DNA (a) is fragmented by the addition of a restriction enzyme (biological catalyst that "cuts" DNA at specific sites).
- 2 The fragments are then separated, according to their length, into invisible bands (b) on electrophoresis gel (c).
- 3 The separated DNA fragments can be then be transferred to a nitrocellulose membrane (d). The DNA molecules are made to stick permanently to the membrane.
- 4 When a radioactive DNA probe solution (e)

is added to the membrane and then gently washed off, some of the probes will remain attached to any DNA bands that have a complementary sequence.

- 5 The membrane (d) is placed against a photographic film (f).
- 6 The film darkens (g) wherever the radioactive DNA probe has bound to the membrane. The probe has identified which DNA fragment contains the complementary DNA sequence for the probe.

RECOMBINANT HUMAN INSULIN

In 1982, a genetically engineered version of insulin became the first recombinant gene product to be licensed for use in humans. Insulin is a hormone (regulatory chemical) needed by people who suffer from the disease diabetes mellitus. It controls the level of glucose (a sugar) in the blood.

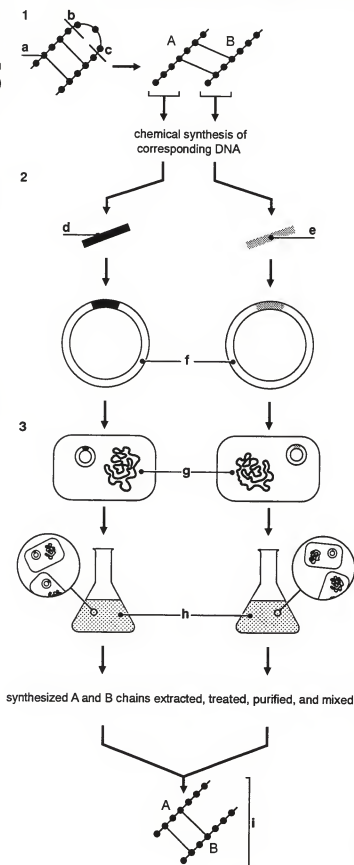
1 During the synthesis of insulin in humans, its protein chain (a) is cut at two positions (b and c) and the middle portion of the chain is lost, so that insulin finally comprises two protein chains:

- an A chain of 21 amino acids (protein building blocks), and
- a B chain comprising 30 amino acids.

The chains are still linked by two disulphide bonds.

2 DNA (deoxyribonucleic acid) molecules (d and e) corresponding to each insulin chain are chemically synthesized. Each of these is inserted into an *E. coli* plasmid (DNA molecule separate from the bacterial chromosome) (f).

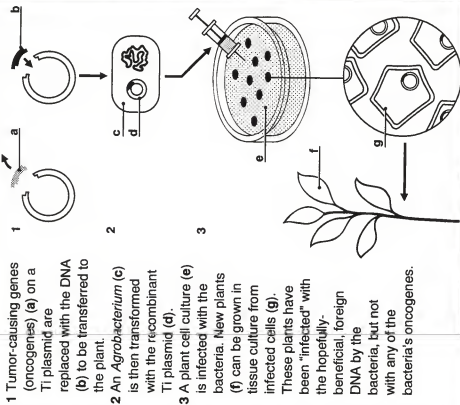
3 *E. coli* bacteria (g) are transformed with the two insulin-containing plasmids and large bacterial cultures (h) grown. The bacteria synthesize the insulin proteins, which can then be purified. When the A and B chains are mixed together, human insulin (i) is produced. It is called recombinant human insulin because it is produced using recombinant DNA technology.



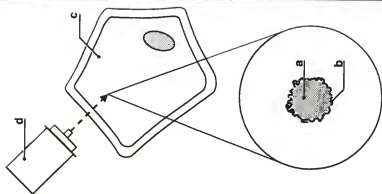
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TRANSGENIC ORGANISMS 1: PLANTS

B Another way to get DNA into plant cells is to use the bacterium *Agrobacterium tumefaciens*, which infects many plants (but not cereal crops), causing tumors. The tumors are caused by a plasmid (DNA molecule separate from the bacterial chromosome) called the Ti plasmid, which these bacteria carry.



A Minute tungsten beads (a) are coated with DNA (b) and then fired at high speed into the plant cells (c) using what is, in effect, a microscopic gun (d).



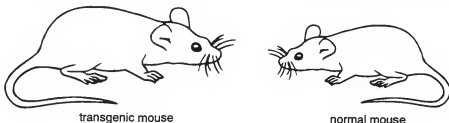
Transgenic organisms are those that contain some DNA (deoxyribonucleic acid) from another species. In the past, selective breeding was used to improve crops and herds. This process was prolonged and ineffectual. By identifying, isolating, and transferring to a new host only the genes needed, however, dramatic improvements can potentially be achieved much faster. The first transgenic food to be licensed for consumption was a tomato. The insertion of genes from another plant species gave improved flavor and ripening characteristics.

Making transgenic organisms requires two things:

- firstly, DNA must get into the organism's cells; and
- secondly, the DNA must integrate with the host cell's chromosomes so that it can be transferred to daughter cells after cell division. The cell wall of a plant cell usually prevents it from taking up DNA. There are several ways to get round this problem (A and B).

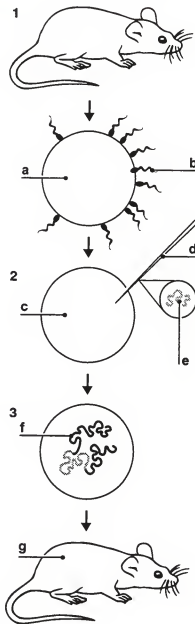
TRANSGENIC ORGANISMS 2: ANIMALS

One of the first transgenic animals was produced in 1982 by Richard Palmiter (born 1942) and Ralph Brinster (born 1932). They joined the growth hormone gene from rats to the promoter of a gene that mice express when they eat zinc. The mice they produced contained this DNA, and when they were fed zinc they grew three times faster than normal mice and ended up more than twice as heavy because of the increased amounts of growth hormone they synthesized.

**Producing a transgenic animal**

- 1 Egg cells (a) are removed from a female animal and fertilized with sperm (b).
- 2 Before the gamete (sex cell) nuclei (control centers) can fuse, the fertilized egg (c) is immediately injected. The tiny syringe (d) used has about 2 picoliters (2 million millionths of a liter) of a solution containing the foreign DNA (e).
- 3 If the injected DNA is incorporated in the cell's chromosomes (f), then the egg develops into an animal (g) with a copy of the foreign DNA in each of its cells.

This technique has led to the production of transgenic mice, sheep, pigs, and cattle.



RFLPs

When DNA (deoxyribonucleic acid) from an individual is digested with a restriction enzyme (biological catalyst that "cuts" DNA at specific sites), it is cut into a certain number of fragments. DNA from another individual, however, might be cut into a different number of fragments by the same restriction enzyme. This is because although the restriction enzyme always cuts at the same DNA base sequence, this sequence will appear at diverse places and a varying number of times in the DNA of different individuals. Variations from one individual to the next are called RFLPs (restriction fragment length polymorphisms). RFLPs can be treated as genetic markers and used in mapping genes and DNA fingerprinting (see 6.49).

1 Cutting the DNA

The same restriction enzyme (a) is used to cut the DNA (b and c) from different individuals, digesting the DNA into fragments (d).

2 Southern blotting

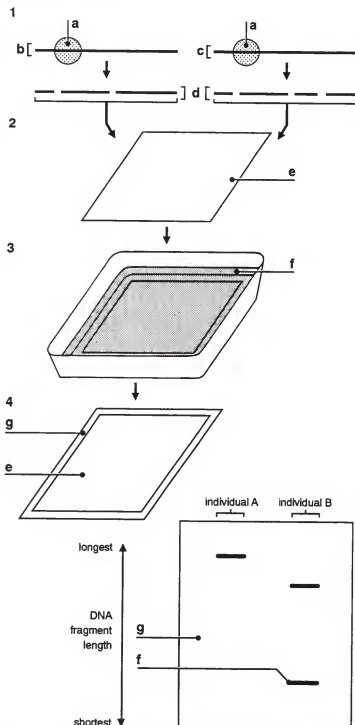
These fragments are separated, according to their length, into invisible bands by gel electrophoresis and then transferred to a nitrocellulose membrane (e). This process is known as Southern blotting.

3 DNA probe

The membrane is then soaked with a radioactive DNA probe solution (f). This probe will bind to any DNA on the membrane that has a complementary base sequence. Unbound probes are washed off.

4 Results

The membrane is placed against a photographic film (g), which darkens wherever radioactivity is present. Therefore, the bands (f) on the photographic film indicate where on the membrane the radioactive probe bound. Because the DNA in the region that binds the probe is cut a different number of times when comparing the two individuals, different fragment lengths are shown up by the probe. These are the RFLPs.

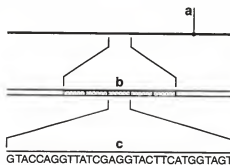


DNA FINGERPRINTING 1

DNA (deoxyribonucleic acid) fingerprinting (or genetic fingerprinting) is an example of the use of sophisticated biochemical techniques in the analysis of genetic material.

VNTRs

Part of the DNA (a) of each individual is hypervariable, meaning that it varies greatly between unrelated individuals. Such regions (b) contain repeated sequences (c) in which the number of repetitions varies between individuals. These regions are called VNTRs (variable number tandem repeats). VNTRs vary in length between individuals because of their differing numbers of repeats. In practice, this enables them to be used to make a DNA fingerprint that identifies a person almost uniquely.

**PRODUCING A DNA FINGERPRINT**

1 VNTRs (a) can be amplified (copied many times) (b) from a very small tissue or body-fluid sample by PCR (the polymerase chain reaction) (see 6.40).

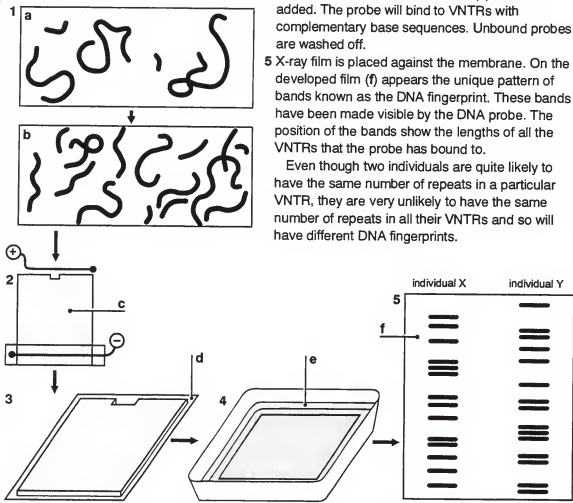
2 Using gel electrophoresis, the copied VNTRs are separated, according to their length, into invisible bands in an agar gel (c).

3 The bands containing the VNTRs are transferred to a nitrocellulose membrane (d).

4 A radioactive DNA probe solution (e) is then added. The probe will bind to VNTRs with complementary base sequences. Unbound probes are washed off.

5 X-ray film is placed against the membrane. On the developed film (f) appears the unique pattern of bands known as the DNA fingerprint. These bands have been made visible by the DNA probe. The position of the bands show the lengths of all the VNTRs that the probe has bound to.

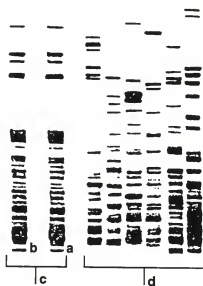
Even though two individuals are quite likely to have the same number of repeats in a particular VNTR, they are very unlikely to have the same number of repeats in all their VNTRs and so will have different DNA fingerprints.



DNA FINGERPRINTING 2

LINKING AN INDIVIDUAL TO THE SCENE OF A CRIME

A sample of DNA for analysis can be extracted from a blood stain, semen sample, hair, fingernail scraping, or a small sample of tissue from the scene of a crime. The DNA fingerprint from a scene-of-crime sample (a) is compared with that taken from a suspect (b). If there is a match, as in this case (c), the suspect could be linked to the scene of the crime. The DNA fingerprints of other suspects (d) do not match the scene-of-crime sample.

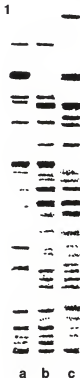


ESTABLISHING FAMILY RELATIONSHIPS

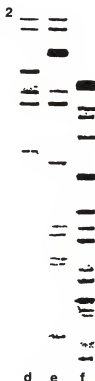
DNA fingerprinting can be used in cases involving the issue of paternity or maternity. Parenthood can be established to a high degree of probability, but not absolutely. An individual's mother and father have in common about half of the person's DNA. An individual's genetic fingerprint will thus have several regions that match each of their parents. This would not be the case were the individuals unrelated.

Proving and disproving parenthood: two examples

1 A woman (a) who claims to be the biological mother of an adopted child (b) is shown to be closely related to him. The biological father's DNA fingerprint (c) has different bands matching other bands found in the child's DNA fingerprint. The mother's claim is, therefore, likely to be true.



2 A woman (d) claims that her child (e) is the son of a famous rock star (f). A comparison of their DNA fingerprints shows, however, that the rock star is not closely related to the child. The woman's claim is disproved.



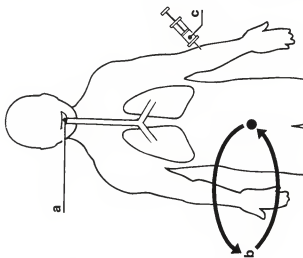
GENE THERAPY 1

Gene therapy involves inserting a healthy gene into a human body to replace or augment the functioning of a faulty gene. This technique promises to be particularly useful for alleviating certain inherited diseases involving gene mutations such as cystic fibrosis, hemophilia, and thalassemia.

REPLACING FAULTY GENES

One of the major technical problems in gene therapy is getting a new gene into the cells that need it. Three of the main methods currently being developed are listed in the table below.

METHOD OF APPLICATION	EXAMPLE OF DISEASE TREATED	METHOD OF GENE THERAPY
Aerosol spray (a) is used to deliver the new gene to the diseased lung tissue.	<ul style="list-style-type: none"> cystic fibrosis (in which cells produce mucus that is thicker than normal) 	<ul style="list-style-type: none"> Copies of the healthy gene are applied directly to the surface of the affected cells, so that they take up the new gene. No operation is required.
Diseased cells are removed from the body, copies of the healthy gene inserted into them, and then the cells are returned to the correct place in the body (b).	<ul style="list-style-type: none"> ADA (adenosine deaminase) deficiency (in which the gene producing the ADA enzyme – biological catalyst – is defective, preventing bone marrow from producing healthy white blood cells to combat infections) 	<ul style="list-style-type: none"> Some bone marrow is removed, including stem cells, which later develop into white blood cells; the bone marrow, including stem cells, is treated with the new gene; and the treated cells are returned to the body's bone marrow.
New genes are injected into the bloodstream (c). The genes are programmed to be activated only when they enter specific target cells that have special characteristics.	<ul style="list-style-type: none"> skin cancers (melanomas) (still in exploratory phase) 	<ul style="list-style-type: none"> Genes that cause cancerous cells to self-destruct are injected. Cancerous cells, but not healthy cells, switch on the self-destruct genes.



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GENE THERAPY 2

USING VIRUSES IN GENE THERAPY

Once a healthy human gene has been isolated, using this gene to replace a faulty gene is neither easy nor straightforward. There are two main difficulties:

- getting the "healthy" (normal) gene inside a target cell and
- stopping the healthy gene from being destroyed inside the cell, so that it can start to work and manufacture the gene product (a protein) that is missing or defective.

Both of these difficulties can, in some cases, be overcome with the use of a virus as a vector (carrier). A virus that incorporates its genetic material into the DNA of a host cell is used.

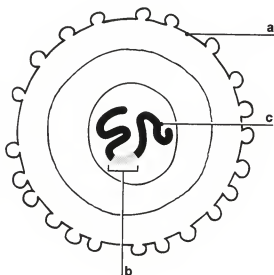
How a virus delivers a gene to DNA

1 The virus (a) is genetically engineered so that a copy of the healthy gene (b) is inserted into the viral DNA. The virus's own genetic material (c) is modified in such a way that the virus cannot multiply and harm the target cells into which it is introduced.

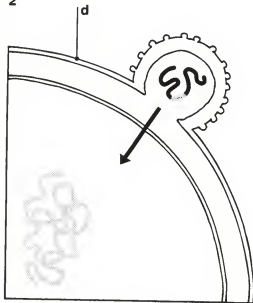
2 The virus is delivered to the patient's target cells by any of the three methods described on 6.51. Once the virus reaches a target cell (d), it readily attaches itself and empties the genetic material into the cell.

3 The healthy gene is then incorporated into the cell's DNA (e) and begins to manufacture the gene product (f) that corrects the patient's condition.

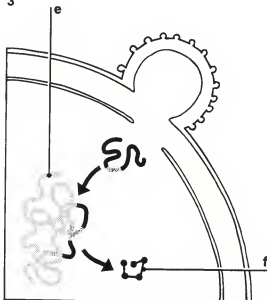
1



2



3



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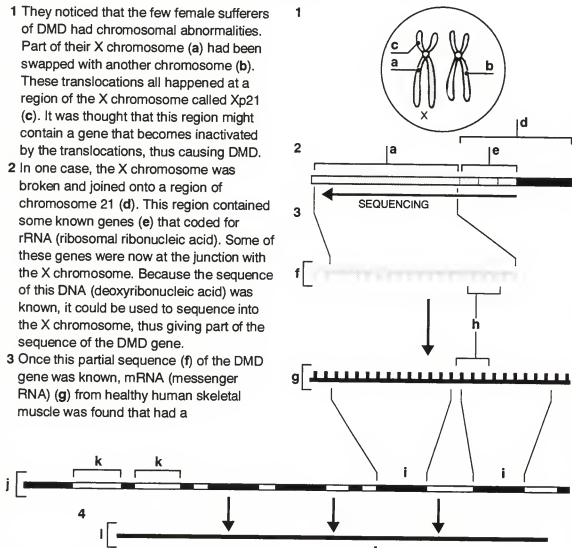
FINDING THE GENE FOR MUSCULAR DYSTROPHY

DMD (Duchenne muscular dystrophy) is a rare disease affecting mainly boys. It causes their muscles to progressively waste away. Little was known about the cause of the disease until the work of Ronald Worton (born c. 1943) and his co-workers in the mid-1980s.

1 They noticed that the few female sufferers of DMD had chromosomal abnormalities. Part of their X chromosome (a) had been swapped with another chromosome (b). These translocations all happened at a region of the X chromosome called Xp21 (c). It was thought that this region might contain a gene that becomes inactivated by the translocations, thus causing DMD.

2 In one case, the X chromosome was broken and joined onto a region of chromosome 21 (d). This region contained some known genes (e) that coded for rRNA (ribosomal ribonucleic acid). Some of these genes were now at the junction with the X chromosome. Because the sequence of this DNA (deoxyribonucleic acid) was known, it could be used to sequence into the X chromosome, thus giving part of the sequence of the DMD gene.

3 Once this partial sequence (f) of the DMD gene was known, mRNA (messenger RNA) (g) from healthy human skeletal muscle was found that had a



complementary base sequence (h). This mRNA yielded the sequence of all the protein-coding regions (exons) (i) of the DMD gene.

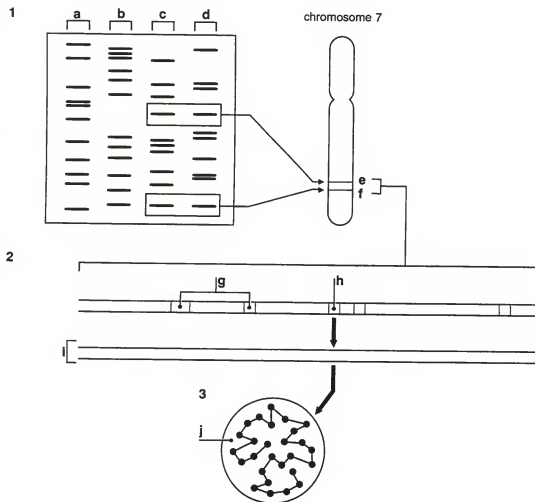
Louis Kunkel (1946–95) and others completed sequencing the whole gene (j). It was found to be enormous: over 2.5-million-nucleotides (DNA building blocks) long and with more than 65 introns (nonprotein-coding parts) (k).

4 The mRNA (l) produced by the DMD gene encodes for a large protein molecule called dystrophin (m). Sufferers of DMD have an inactive DMD gene and lack this protein.

Now that the DMD gene has been identified, it may be possible one day to provide patients with a working dystrophin gene through gene therapy.

FINDING THE GENE FOR CYSTIC FIBROSIS

In 1990, Lap-Chee Tsui (born 1950) and colleagues located the gene for cystic fibrosis. This is a potentially debilitating condition that leads to the production of mucus (thick, slimy fluid) in the lungs that is thicker than normal. The gene for cystic fibrosis was found without any clues such as chromosomal rearrangements to point to its location. All that was known was that the disease was likely to be caused by the mutation of a single gene.



1 First, the gene was localized to a particular chromosome using RFLP analysis (see 6.48) of families with more than one unaffected member (a and b) and more than one affected member (c and d).

On chromosome 7, two RFLPs (e and f) located 1.5 million nucleotides (DNA building blocks) apart were shown to flank either side of the disease-causing gene.

2 Small regions of DNA (deoxyribonucleic acid) (g) in this part of chromosome 7 were sequenced – that is, the order of bases was determined. One sequence (h) was found

that looked very much like the start of a gene. This was used as a DNA probe to locate complementary mRNA (messenger ribonucleic acid) (i) in the ducts of a sufferer's sweat glands.

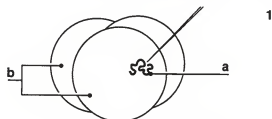
3 The sequence of this mRNA was used to work out the sequence of the gene product (a protein) (j). This protein was proved to be associated with cystic fibrosis because sufferers, but not nonsufferers, had a mutated form. It follows that cystic fibrosis is caused by mutations in the gene that produces this protein.

KNOCKOUT MICE AND CYSTIC FIBROSIS

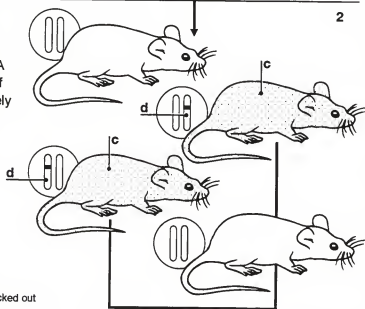
In order to develop treatments for diseases it can be useful to have animal models on which to experiment. It is possible to produce mice that have a particular gene deleted or mutated. A mouse model for cystic fibrosis (a disease that leads to the production of mucus that is thicker than normal) has been developed. The cystic fibrosis gene in a mouse was altered so it would have the same DNA (deoxyribonucleic acid) sequence as the mutant genes of afflicted humans.

1 Microinjection

The first step is to inject the disease-causing human cystic fibrosis DNA (a) into mice embryos (b).

**2 First generation**

Tissue samples from the newborn mice are tested to find the ones (c) that have a copy of the foreign DNA replacing the original DNA in one of their chromosomes. It is very unlikely that any of these first generation mice will have both copies of their original genes replaced – one on each homologous (matching) chromosome (d).

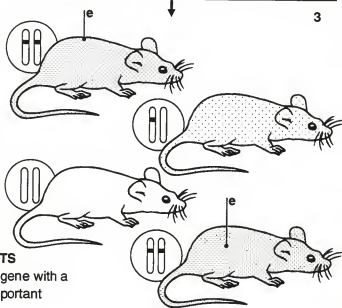


Key:

- Mouse with unaffected DNA
- Mouse with one knocked-out gene
- Mouse with both copies of gene knocked out

3 Second generation

The third step is to interbreed this first generation of transgenic mice so that some of the offspring (e) will be homozygous for the inserted gene – that is both copies of the original gene have been replaced. These mice are the experimental models for treating cystic fibrosis in humans. Their original gene has been “knocked out” and replaced by the disease-causing cystic fibrosis gene.

**IMPLICATIONS OF GENE KNOCKOUTS**

The ability to knock out a dysfunctional gene with a functional one could potentially have important applications in gene therapy.

© DIAGRAM

GENOME PROJECTS

A genome is an organism's complete set of genetic information. In a bacterium, this comprises a single, circular chromosome; in a human, it comprises all 46 linear chromosomes. Genome projects are the cooperation of many research groups to determine the base sequence of an organism's entire genome. Several organisms are the subjects of genome projects and the genomes of some have already been completely sequenced.

ORGANISM	TYPE	SIZE OF GENOME (millions of base pairs)	SEQUENCED BY 1997
<i>E. coli</i>	eubacterium	4.7	x
<i>M. jannashii</i>	archaebacterium	1.7	✓
<i>S. cerevisiae</i>	yeast	125	✓
<i>A. thaliana</i>	flowering plant	100	x
<i>C. elegans</i>	round worm	100	x
<i>D. melanogaster</i>	fruit fly	120	x
<i>M. musculus</i>	mouse	3,000	x
<i>H. sapiens</i>	human	3,000	x

HUMAN GENOME PROJECT

The Human Genome Project was launched in 1990 by James Watson (born 1928) of Watson and Crick fame (see 6.07). It is not expected to be completed until well into the twenty-first century.

Physical mapping

The first major goal is to construct physical chromosome maps (see 6.57). This involves mapping 24 chromosomes (A).

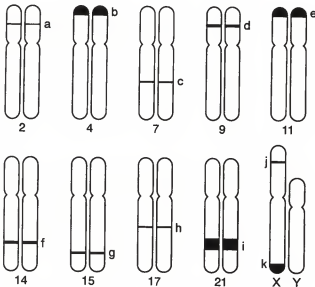
Correlation

These physical maps will then be correlated with a linkage map constructed using more traditional gene mapping techniques (see 5.17).

DNA sequencing

The final stage is to determine the entire DNA (deoxyribonucleic acid) sequence. There are three billion base pairs in the human genome, which have been estimated to form between 50,000 to 100,000 genes.

A Depicted below are the locations of some disease-causing genetic mutations that have already been mapped.



- | | |
|-------------------------|-------------------------------------|
| a Familial colon cancer | g Tay-Sachs disease |
| b Huntington's disease | h Breast cancer |
| c Cystic fibrosis | i Lou Gehrig's disease |
| d Skin cancer | j Duchenne muscular dystrophy (DMD) |
| e Sickle-cell anemia | k Hemophilia |
| f Alzheimer's disease | |

Human chromosomes fall into 23 homologous (matching) pairs. These pairs are numbered 1 to 22 with the last pair – the sex chromosomes – called X and Y. As both homologues of a pair carry the genes for the same traits, only one from each pair needs to be mapped. Both the sex chromosomes need to be mapped, however, as they carry different genes.

Concerns about the Human Genome Project

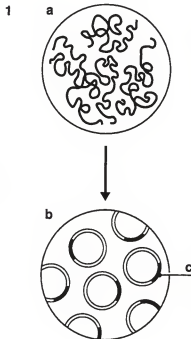
- Some people fear that this huge project will detract funds from other branches of biology.
- Another worry is that the knowledge could be abused, perhaps even leading to the genetic engineering of humans.

PHYSICAL GENE MAPPING

Physical maps give the locations of genes on chromosomes. There is generally a good correlation between the results achieved by a physical map and a linkage map (see 5.17).

CONSTRUCTING A PHYSICAL MAP**1 Creation of a DNA library**

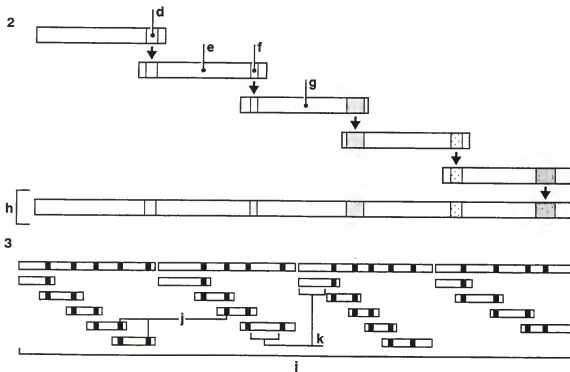
The genome (complete set of genes) (a) of an organism is cloned (see 6.42) to create a DNA library (b). This is a collection of recombinant DNA (deoxyribonucleic acid) molecules (c), each containing part of the original DNA.

**2 Chromosome walking**

The base sequence of a region (d) at the end of one clone is determined. This is used as a probe to find an overlapping clone (e). A region (f) at the other end of this clone can then be sequenced and used as a probe to find the next clone (g). This can be continued until a whole chromosome (h) is covered.

3 The physical map

When a chromosome has been "walked," a collection (i) of ordered, overlapping DNA clones has been created. The regions of known sequences (j) comprise the physical map. The lengths of the rest of the chromosome fragments (k) can then be measured even though their exact sequences are not known.

**APPLICATIONS**

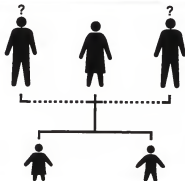
- Physical maps are used in genome projects, which attempt to determine the base sequence of an organism's complete set of genes.
- Physical maps can be used to locate particular target genes and other markers.

APPLICATIONS OF ANALYTICAL DNA TECHNOLOGY

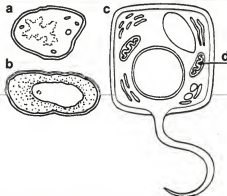
The applications of analytical DNA (deoxyribonucleic acid) technology are wide ranging.

FORENSIC SCIENCE

DNA sequencing (see 6.38), PCR (the polymerase chain reaction) (6.40), RFLPs (restriction fragment length polymorphisms) (see 6.48), and DNA fingerprinting (see 6.49) are used to analyze plant and animal pedigrees – including sorting out human paternity or maternity disputes – and to pick out the perpetrators of crimes or establish the innocence of other people.

**TAXONOMY**

The sequencing of DNA that has been conserved during evolution – such as the genes for rRNA (ribosomal ribonucleic acid) molecules – has led to improved classifications of life forms. For example, it has been confirmed that the archaeobacteria (a) and eubacteria (b) are genetically as different from one another as they are from eukaryotic cells (c), and that mitochondria (d) are probably derived from ancient eubacterial cells.

**MEDICINE**

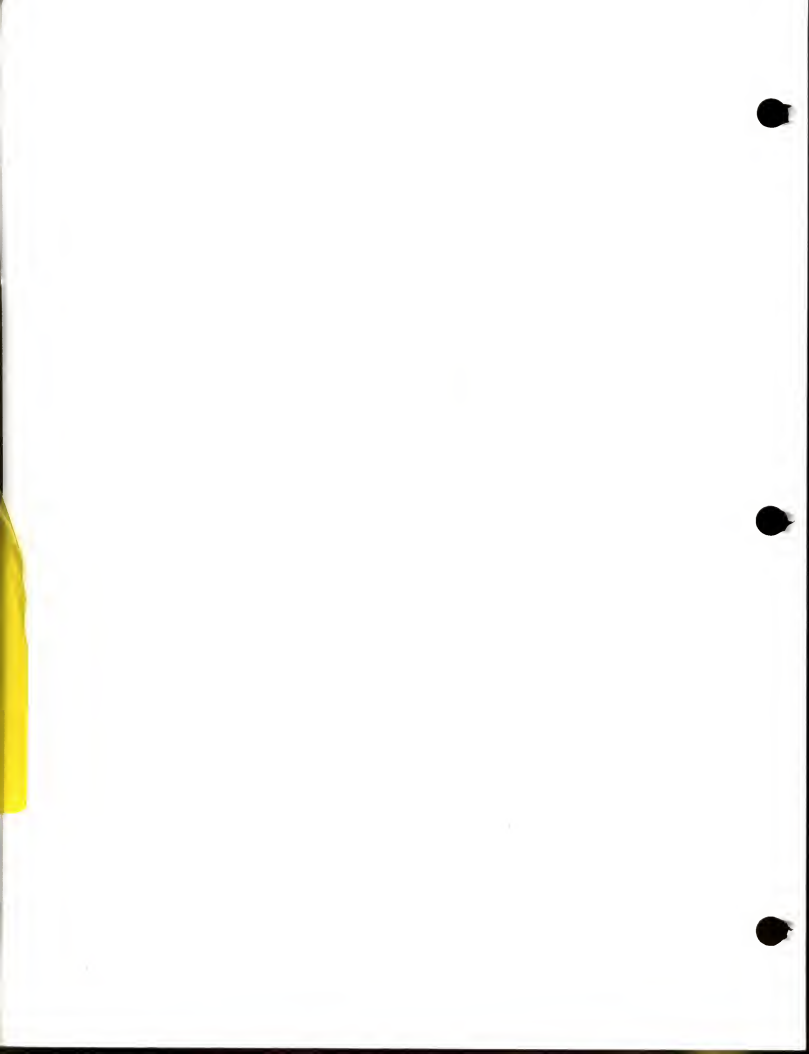
DNA sequencing, PCR, and RFLPs are used to diagnose disease-causing genetic defects, even before birth, and bacterial and viral infections.

**SPECIES IDENTIFICATION**

Species can be identified and tested for using PCR and DNA probes. Food products such as meats can be tested for their animal of origin – for example, to detect the presence of horse meat in beef products.

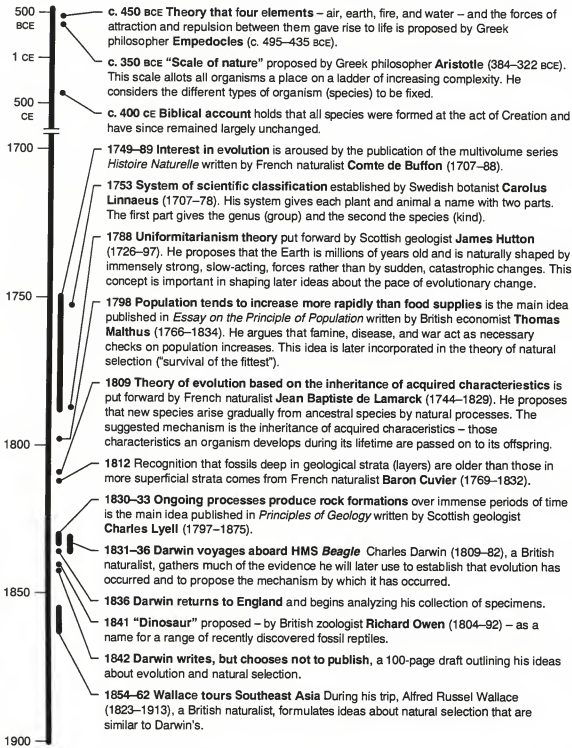


7. POPULATION GENETICS
AND EVOLUTION



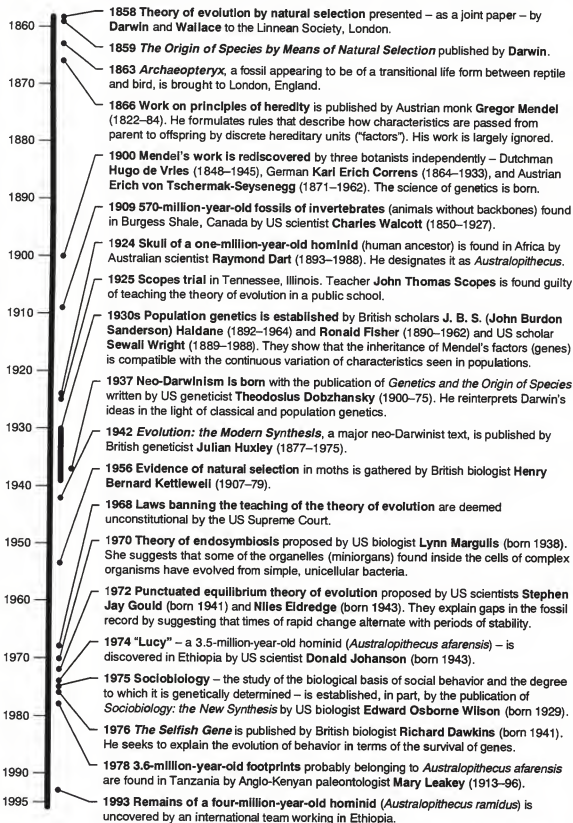
CONCEPTS OF EVOLUTION THROUGH THE AGES 1: c. 450 BCE – 1862 CE

The concept of evolution – that the Earth's structure and its life forms have changed over time – is still a new idea. The influence of classical Greeks, coupled with literal interpretations of the Bible, stifled any debate about evolution until the mid-1700s. At that time, geologists were discovering that the Earth was much older than previously thought. Also, fossil finds indicated that some species were long extinct while others had arisen fairly recently. By the early 1800s, scientists were beginning to recognize that evolution had occurred. The religious and intellectual climate meant, however, that many were reluctant to publish their findings.



CONCEPTS OF EVOLUTION THROUGH THE AGES 2: 1858–1993

Darwin's *The Origin of Species* (1859) brought the idea of evolution to a wider public. Despite great controversy, evolution was gradually accepted by scientists. By the 1940s, neo-Darwinism was able to explain natural selection in terms of the selection of genes within populations.



CONCEPTS OF EVOLUTION BEFORE DARWIN

The concept of evolution – that the Earth's structure and its life forms have changed over time – is still a comparatively new idea. Early Greek philosophers – notably Empedocles (c. 495–435 BCE) and Aristotle (384–322 BCE) – believed fossils were evidence of former life forms that had been destroyed by natural catastrophes. During the Middle Ages in Europe (c. 476–c. 1450 CE), speculation about evolution was considered heresy as it contradicted the biblical account of the Creation. In the mid-1600s, the Irish Archbishop of Armagh, Ireland, James Ussher (1581–1656) fixed the year of Creation at 4004 BCE. By the mid-1700s, however, geological and fossil evidence was challenging this timescale. In 1778, for example, the French naturalist Comte de Buffon (1707–88) estimated that the Earth was nearly 170,000 years old.

The theory of evolution based on the inheritance of acquired characteristics

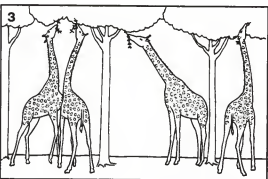
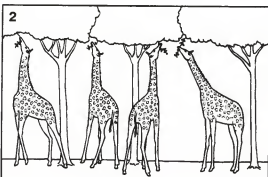
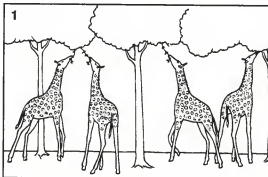
In 1809, the French naturalist Jean Baptiste de Lamarck (1744–1829) formulated the first clear and comprehensive theory of evolution. He made a convincing case that fossils were the remains of extinct animals. Lamarck argued that present-day life forms evolved from preexisting forms by the inheritance of acquired characteristics. According to his theory:

- Organisms strive to meet the demands of their environment and, in the process, they acquire new characteristics.
- These characteristics are then inherited by their offspring, so producing gradual change over time.

The classic example used to explain this theory is the giraffe:

- 1 According to Lamarck's theory, short-necked, ancestral giraffes had to stretch their necks in order to reach the leaves of the trees on which they fed. This had the result of slightly lengthening their necks.
- 2 The offspring of these giraffes inherited these slightly longer necks which they, in turn, stretched during feeding.
- 3 Over many generations, these changes accumulated to produce the long necks of present-day giraffes.

Lamarck's theory has been tested numerous times over the last two centuries. There is almost no evidence in support of it. Were his theory true, for example, then the children of weightlifters would inherit the strong musculature of their parents.



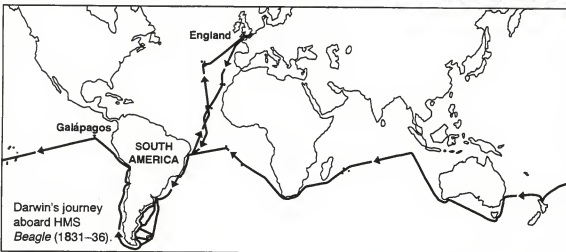
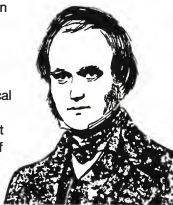
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CHARLES DARWIN

Charles Darwin (1809–82), sometimes called the “Father of Modern Biology,” is without doubt the name best associated with biological evolution – the gradual change of species over time.

Aboard HMS *Beagle*

After an undistinguished academic career as a theology and medical student at Cambridge University, England, Darwin accepted an unpaid post as naturalist on the survey ship HMS *Beagle*. He spent the next five years (1831–36) on a round-the-world trip. The bulk of this time was spent charting and collecting specimens from the east coast of South America. The *Beagle* returned to England in October 1836 via the Galápagos and other Pacific islands.



Back in England

On his return to England, Darwin settled down to a lifetime of meticulous observation, study, analysis, and writing. By 1838, he had formulated the theory of evolution by means of natural selection (sometimes dubbed “survival of the fittest”). It was based on observations that he made during his trip aboard the *Beagle* and drew on the ideas of predecessors such as Thomas Malthus (1766–1834) and Charles Lyell (1797–1875) (see 7.01).

Darwin spent the next twenty years gathering evidence to support his theory of evolution. The huge delay in publishing his ideas was ended in 1858 when he received a letter from Alfred Russel Wallace (1823–1913). Wallace, a British naturalist, had independently come to similar conclusions for the mechanism of evolution – natural selection. By gentlemanly agreement, Darwin and Wallace presented a joint paper at the Linnean Society, London, outlining their ideas. The following year, in November 1859, Darwin

published his seminal book *The Origin of Species by Means of Natural Selection*.

Darwin's achievements

Darwin's major achievements were twofold. Not only did he gather a great deal of evidence in support of evolution, he proposed a plausible theory explaining the mechanism by which species had changed. His ideas about evolution and natural selection have stood the test of time and are still widely accepted by biologists today, though with some modifications.

Darwin expanded his idea that humans and apes shared a common ancestor in his 1871 book, *The Descent of Man*. This was one of the most hotly debated aspects of his theory of evolution and attracted much ridicule, as in this cartoon.



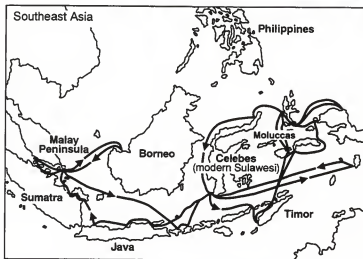
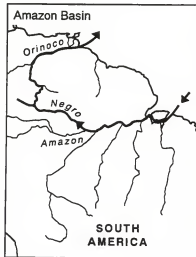
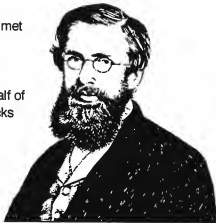
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ALFRED RUSSEL WALLACE

Alfred Russel Wallace (1823–1913), while not as well known as Charles Darwin (see 7.04), should be given due credit for formulating the theory of evolution by natural selection – the gradual change of species over time due to what Wallace termed “survival of the fittest.”

Wallace's voyages

While working as a teacher in Leicester, England, Wallace met the famous British naturalist and explorer Henry Bates (1825–92). He later joined Bates on a four-year expedition (1848–52) to the Amazon Basin. During this expedition, Wallace collected nearly 15,000 animal specimens, over half of which were new to science. Wallace was beset with setbacks and difficulties. During the expedition, he suffered from malaria and other tropical diseases. On the return journey in 1852, the ship sank and all his specimens and most of his notes were lost. Undaunted, he set off in 1854 for what was to prove to be an eight-year expedition to the Malay Archipelago and other parts of Southeast Asia.

**Theory of evolution by natural selection**

In 1858, while he lay ill in bed with malarial fever, ideas about natural selection came to Wallace. He put them down on paper in a 12-page letter to Darwin that asked for Darwin's opinion and requested that he forward the letter to the geologist Charles Lyell (1797–1875). Wallace was unaware that Darwin had, some twenty years earlier, pieced together the same ideas but had since failed to publish them. The receipt of Wallace's letter was sufficient to spur Darwin into action, and the two men outlined their ideas in a joint paper presented at the Linnean Society, London, later that year. While Darwin's book *The Origin of Species by Means of Natural Selection* was published the following year (1859), Wallace did not publish his book on the subject – *Contributions to the Theory of Natural Selection* – until 1870.

Wallace's achievements

Unlike Darwin, Wallace did not have any formal training in biology. Like Darwin, however, he gained knowledge and experience in the field, through reading, and in discussions with naturalists and geologists. Apart from being the original copresenter of the theory of evolution by natural selection, Wallace was a strong proponent of social reform in Victorian England. He also established the field of biogeography – the geographical distribution of organisms within distinct zones of the world.

THE THEORY OF EVOLUTION BY NATURAL SELECTION

In his 1859 book *The Origin of Species by Means of Natural Selection*, the British naturalist Charles Darwin (1809–82) put forward his theory of natural selection.

Darwin's main propositions

- Organisms overproduce: they tend to produce more offspring than the environment can support.
- In the long term, despite this overproduction, population sizes tend to remain fairly constant or fluctuate around an average value.
- There is variation within a population, that is, individuals differ from one another.
- Some of these variations are inherited characteristics – they are passed on from one generation to the next.

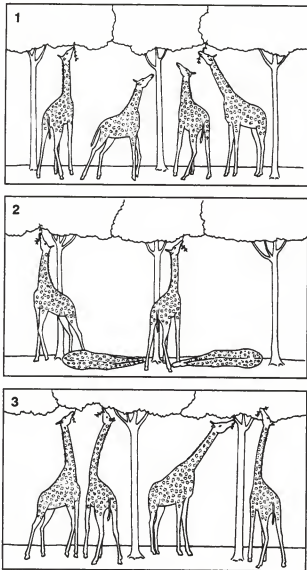
Darwin's main deductions

- Largely due to overproduction, there is a “struggle for existence” between individuals. Some survive to reproduce and others do not. This struggle regulates population numbers.
- Some variations have survival value. Individuals with these variations are more likely to survive and reproduce, passing on their characteristics to their offspring. This is natural selection.
- Over time, natural selection might lead to populations with individuals having many features that have survival value. In this way, species can slowly change (evolve), or even give rise to new species.

NATURAL SELECTION IN ACTION

- 1 Using the giraffe as an example, some ancestral giraffes were short-necked and others slightly longer-necked. This occurred simply because there is variation within a population.
- 2 Those giraffes with longer necks could reach foliage more easily and at higher levels than those with shorter necks. The short-necked ones were, therefore, more likely to die because they lost out in competition and became malnourished.
- 3 Those giraffes with longer necks, however, were more likely to survive and pass on their characteristics to subsequent generations. Due to this natural selection, the population would eventually come to contain only giraffes with long necks.

The weakest points in Darwin's theory were the lack of satisfactory explanations as to how variation arose in the first place and how it was passed on from one generation to the next. Had he read the work of Austrian monk Gregor Mendel (1822–84) on the principles of inheritance, however, Darwin could have added further weight to his ideas. The blossoming of genetics in the 1900s has provided abundant evidence to support Darwin's theory in its broadest principles.



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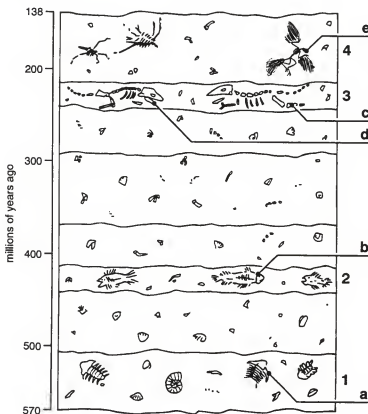
TRADITIONAL EVIDENCE FOR EVOLUTION 1: THE FOSSIL RECORD (1)

Clear evidence for evolution comes from examining the fossil record. In older geological strata (layers) only the fossils of simple life forms are found. In more-recent strata, however, all manner of life forms, both simple and complex, are found. The implication is that simpler life forms have given rise to the vast variety of organisms found on Earth today.

EXAMPLE OF A FOSSIL RECORD

In practice, a full fossil sequence is not found at any single geographic location, but is pieced together from evidence at many sites.

- 1 In Cambrian rocks 500–c. 570 million years old only relatively simple organisms such as trilobites (a) are found.
- 2 410–435-million-year-old rocks of the Silurian Period show the first signs of jawed fish (b).
- 3 The first dinosaurs (c) and mammals (d) are not found until deposits of the Triassic Period, which dates from 205–240 million years ago.
- 4 Birds (e) are not evident until the Jurassic Period, 138–205 million years ago.



DATING FOSSILS

- Rough dating of sedimentary rocks (and the fossils contained in them) can be obtained by estimating the time taken for sedimentary deposits to be laid down over many millions of years.
- More accurate dating can be achieved by analyzing radioactive elements associated with fossil finds. Radioactive elements decay at a constant rate and so can provide a "radioactive clock" that measures time.

Potassium-argon dating

The potassium-argon method of dating is commonly used to date fossils that are many millions of years old. Igneous rock is formed from molten material beneath the Earth's surface. Once it has formed, the radioactive clock of its constituents starts to tick. The ratio of the radioactive element potassium-40 to its breakdown product, argon-40, is used to give a measurement of age. Potassium-40 is chosen as it decays very slowly (it has a half-life of 1.3 billion years) and is found in many types of rock.

Carbon dating

Carbon dating is used to date fossilized material up to about 50,000 years old. Organic (carbon-based) material in fossils can be dated by assessing the amounts of radioactive carbon-14.

TRADITIONAL EVIDENCE FOR EVOLUTION 2: THE FOSSIL RECORD (2)

The fossil record depicting the evolution of the modern horse is one of the best documented fossil transitions. The fossil sequence from the doglike *Hyracotherium* of more than 30 million years ago to the modern horse *Equus* is shown here in simplified form. Nowhere is the entire fossil record present in one geographical location.

Evolutionary trends

The fossil sequence from *Hyracotherium* to *Equus* shows three clear evolutionary trends:

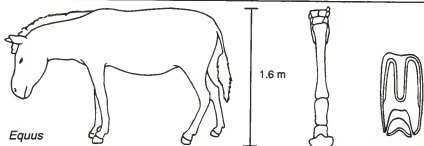
- an increase in body size;
- a reduction in the number of toes (digits) in

contact with the ground; and

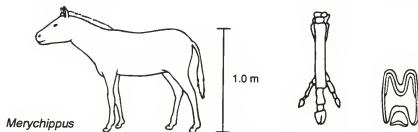
- an enlarging and strengthening of the teeth and increased folding of their grinding surfaces.

EPOCH (dates)

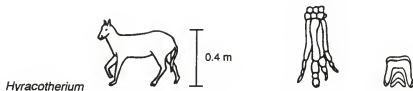
Pliocene on
(from 5 million
years ago)



Miocene
(5–24 million
years ago)



Eocene
(38–55 million
years ago)

**Changing environments and evolution**

These evolutionary trends have been related to changing environmental conditions.

Eocene Period *Hyracotherium* lived in the marshy, wooded countryside of the Eocene. Its splayed toes were well adapted for walking on soft ground and its simple dentition was adequate for eating the lush vegetation on which it fed.

Miocene Period By the Miocene, woodland had been largely replaced by open prairie (grasslands). A larger body size and hoofed

limbs were more effective in allowing *Merychippus* to see and then run away from approaching predators. Strong grinding teeth were better able to cope with the higher mineral content of grassland vegetation.

Pliocene Period On the modern horse *Equus* first appeared three million years ago during the Pliocene Period. It is even better adapted to prairie environments than *Merychippus* with an even larger body size and stronger grinding teeth.

TRADITIONAL EVIDENCE FOR EVOLUTION 3: COMPARATIVE EMBRYOLOGY

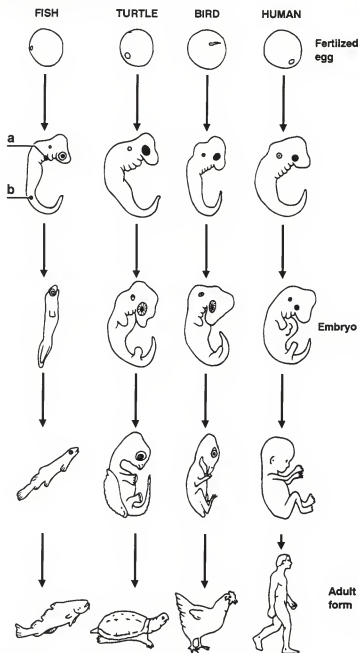
An embryo is an organism in the early stages of development before birth. Embryology is the study of how embryos develop. Comparative embryology shows how the embryos of certain different groups resemble each other at particular stages. Similarities indicate that the groups may share a common ancestor.

COMPARATIVE EMBRYOLOGY OF VERTEBRATES

The embryos of vertebrates (animals with backbones) show striking structural similarities. At comparable stages, the vertebrate embryos shown here all possess:

- **Visceral clefts (a)**, which are retained in adult fish but in other groups become modified for various uses. In mammals, for example, one visceral cleft is retained to become the auditory canal and tube, which are involved in hearing.
- **Segmented muscle blocks** are evident in a tail-like structure (b), which is retained in only some groups.
- **A two-chambered heart (not shown)**, which is retained in fish, but develops into a three- or four-chambered heart in other groups.

This evidence supports the view that all vertebrates descended from an ancestral, fishlike form.



Comparative embryology is actually a specialized form of comparative anatomy – the comparison of structural similarities. Making comparisons between the structures of embryos may show interrelationships not necessarily apparent in the adult form. For example, study of the embryonic and larval development of the more complex invertebrates (animals without backbones) suggests two major evolutionary lineages – protostomes (annelids, mollusks, and arthropods) and deuterostomes (echinoderms and chordates).

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TRADITIONAL EVIDENCE FOR EVOLUTION 4: COMPARATIVE ANATOMY (1)

Apparently dissimilar organisms can sometimes show anatomical (structural) similarities that suggest they evolved from a common ancestor.

HOMOLOGOUS FEATURES

Features that have a similar structure but in different organisms are used for various functions and may look dissimilar are said to be homologous.

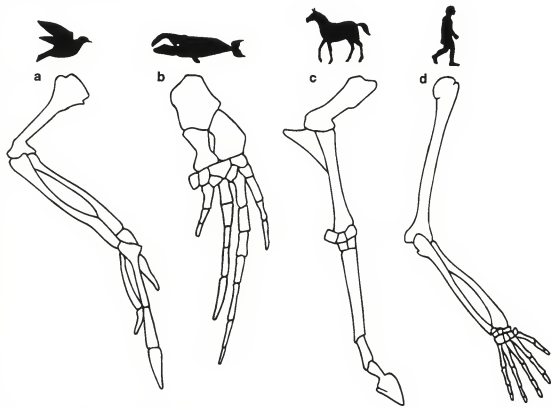
Pentadactyl forelimbs

One of the best examples of a homologous feature is the pentadactyl (five-digit) forelimb. It is found in certain vertebrates (animals with backbones) such as amphibians, reptiles, birds, and mammals.

Examples of pentadactyl forelimbs include:

- a a bird's wing;
- b a whale's flipper;
- c a horse's front leg; and
- d a human arm.

Although these limbs perform different functions and appear to be quite different, they are actually composed of very similar bones, muscles, and nerves. They also share similar origins during development.

**DRAWING CONCLUSIONS BASED ON COMPARATIVE ANATOMY**

Great differences in outer appearance coupled with similarities in underlying structure and design can be explained by evolution:

- Organisms that share many structural similarities may have evolved from a common ancestor.
- Over the years, modifications in the original "design" give rise to the many different forms found in the present day.

For naturalists such as Charles Darwin (1809–82), the very imperfections of design provided some of the most convincing evidence that evolution had occurred. For example, whales have flippers supported by heavy bone rather than the more efficient, lightweight, folding fins of fish. The whale's heavy flippers are derived from the limbs of the land mammals from which they evolved.

TRADITIONAL EVIDENCE FOR EVOLUTION 5: COMPARATIVE ANATOMY (2)

Apparently similar organisms can sometimes show anatomical (structural) differences that suggest they are not closely related.

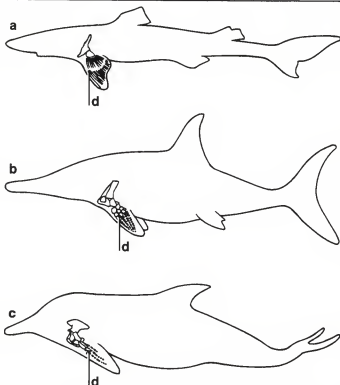
ANALOGOUS FEATURES

Features that look similar and perform comparable functions but do not share the same structure or origin are said to be analogous.

Some examples of organisms that have analogous features are the:

- a** shark (a cartilaginous fish);
- b** ichthyosaur (an extinct reptile); and
- c** the porpoise (a marine mammal).

They all have remarkably similar streamlined bodies with fins. Yet there are significant anatomical differences between them. Their pectoral fins (**d**), in particular, are different structurally. This suggests that they are not closely related. In fact, the fossil record suggests that the three forms arose independently at different times.

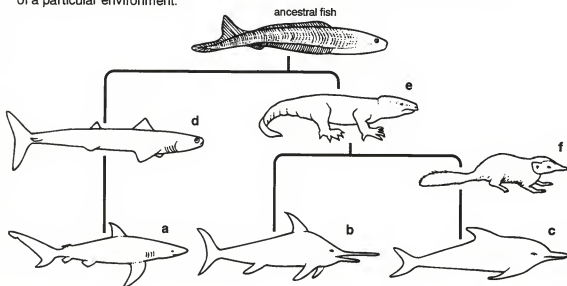


CONVERGENT EVOLUTION

Differences in anatomy coupled with similarities in outward appearance and function can be explained by convergent evolution, in which:

- organisms of different forms have adapted in a similar fashion to respond to the demands of a particular environment.

In this example, the shark (**a**), ichthyosaur (**b**), and porpoise (**c**) all evolved from markedly different, recent ancestral forms – ancestral shark (**d**), ancestral reptile (**e**), and ancestral mammal (**f**) respectively – to become fast swimmers in the marine environment.



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TRADITIONAL EVIDENCE FOR EVOLUTION 6: COMPARATIVE ANATOMY (3)

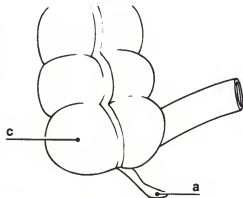
Further anatomical evidence in support of evolution is provided by vestigial structures.

VESTIGIAL STRUCTURES

Structures are said to be vestigial when they serve no useful function but are homologous with larger, useful structures found in other living organisms or ancestral forms. It is thought that vestigial structures once performed a useful function in ancestral forms but have since become more or less redundant

and therefore markedly reduced in size. Well-known human examples of vestigial structures include:

- a the appendix (a small, finger-shaped, outfolding of the gut), and
- b the coccyx (a set of fused bones at the base of the spine).

**Appendix**

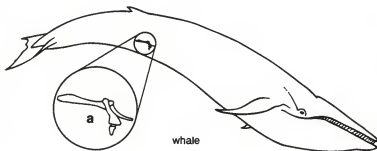
This is a small outfolding of the gut near the junction of the small and large intestines. It is homologous with the part of the cecum (the first part of the large intestine) (c) in which vegetable matter is digested in herbivorous (plant-eating) mammals. The presence of a nonfunctional appendix in humans suggests that our ancestors had a functioning appendix and were herbivores.

**Coccyx**

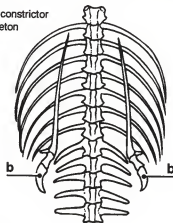
The coccyx is thought to be the remnants of vertebrae (single segments of the spinal column) that once supported a tail. Its presence is consistent with the argument that our evolutionary ancestors had a tail supported by vertebrae.

Other vestigial structures

Other examples of vestigial structures are the remnants of pelvic girdle (a) and hind limb structures (b) found in whales and boa constrictors respectively.



boa constrictor
skeleton



TRADITIONAL EVIDENCE FOR EVOLUTION 7: BIOGEOGRAPHY (1)














Biogeography is the study of the geographical distribution of organisms. Analysis of such distributions provides strong evidence in support of evolution as well as insights into the mechanism by which evolution has occurred.

DARWIN AND THE GALÁPAGOS ISLANDS

In 1835, the British naturalist Charles Darwin (1809–82) visited the Galápagos Islands. The groups lie roughly 900 km (550 miles) west of Ecuador, South America, in the Pacific Ocean. He discovered only 24 species of birds, most of which he had not seen on the mainland; 13 of the species were finches. Darwin proposed that the great variety of finches on the islands could be explained if one original species had evolved into the different types he had observed.

Darwin's finches

The Galápagos finches fall into six main groups comprising 13 different species. The groups can be distinguished by their beak shapes and food preferences. The only species of finch on mainland Ecuador is a ground-dwelling bird that eats seeds (a). On the Galápagos Islands, however, the finches (b to g) exploit a wide range of foods.

	GALAPAGOS FINCH	SHAPE OF BEAK	FOOD PREFERENCES
	b Ground finch		<ul style="list-style-type: none"> ● large and strong (for crushing) ● large seeds 
	c Cactus ground finch		Either: <ul style="list-style-type: none"> ● a relatively straight beak (for probing) with a split tongue, or ● a slightly stouter beak (for cutting). Either: <ul style="list-style-type: none"> ● the nectar of cactus flowers, or ● cactus flesh. 
	d Warbler finch		<ul style="list-style-type: none"> ● slender and pointed (for grasping) ● small insects (caught while in flight) 
	e Insectivorous tree finch		<ul style="list-style-type: none"> ● broad (for grasping) ● small insects (from bark, for example) 
	f Vegetarian tree finch		<ul style="list-style-type: none"> ● curved and parrotlike ● buds ● fruits 
	g Woodpecker (tool-using) finch		<ul style="list-style-type: none"> ● pointed (with which it can hold a cactus spine to use as a tool) ● grubs (speared on tool held in beak) ● small insects (flushed out of tree crevices by tool) 

ADAPTIVE RADIATION

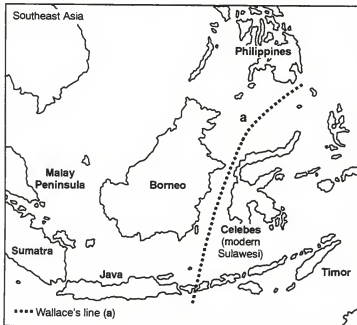
Darwin's finches are an example of adaptive radiation – an ancestral form has evolved into different species that are adapted to new habitats and ways of life. The evidence provided by Darwin's finches supports the view that a seed-eating species of finch arrived from the mainland and colonized the Galápagos Islands some time after they were formed by volcanic action. The arriving birds discovered plenty of space but sparse vegetation. The finches subsequently adapted to exploit a wider range of food sources than seeds alone could provide.

TRADITIONAL EVIDENCE FOR EVOLUTION 8: BIOGEOGRAPHY (2)

The British naturalist Alfred Russel Wallace (1823–1913) largely established the field of biogeography using material he gathered in Southeast Asia and Australasia in the 1850s.

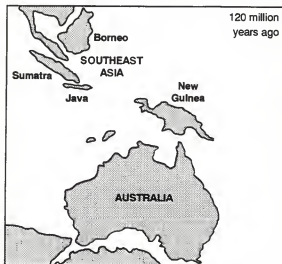
WALLACE'S LINE

Studying nature in Asia and Australasia provided Wallace with some of the evidence he used to formulate his ideas about evolution. During his expeditions, Wallace noted that island bird populations belonged to two different groups. Those northwest of a particular line (now known as Wallace's line) (a) were related to Asian groups, while those southwest were similar to Australian types. He concluded that the two populations on either side of the line had evolved in complete isolation from each other.

**Continental drift**

In Wallace's time the reason for the separate development of these populations was unknown. Current evidence of land movements suggests that 120 million years ago, New Guinea and adjacent islands to the west were nearer Australasia and

farther from Southeast Asia. Meanwhile, the Philippines, Borneo, and Java were nearer mainland Southeast Asia. Over time, the two continents and their associated islands have moved much closer together. This is called continental drift.

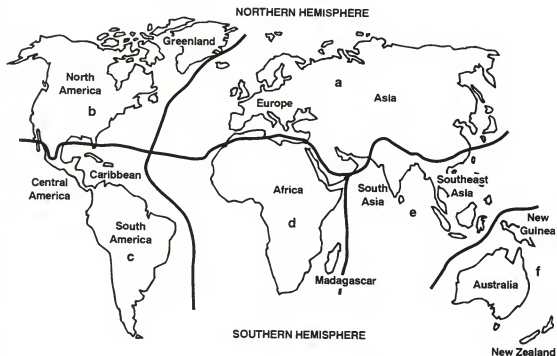


As more evidence has accumulated, it has become apparent that Wallace's line does not represent a true separation between Asian and Australasian species. The boundaries between the animal species of the two continents varies according to the group studied and depends on factors such as the mobility of the animals and their precise routes and rates of colonization.

TRADITIONAL EVIDENCE FOR EVOLUTION 9: BIOGEOGRAPHY (3)

While surveying the worldwide distribution of birds and mammals, Wallace was one of the first to begin to recognize the existence of specific ecological communities of plants and animals in different parts of the world. Today, six regions are recognized as the major biogeographical zones. Each of these regions has its own distinct set of ecological communities.

BIOGEOGRAPHICAL ZONES



In the Northern Hemisphere, there are two biogeographical zones:

- a The Palearctic realm**, which covers Europe, most of Asia, and parts of north Africa; and
- b The Nearctic realm**, which comprises Greenland and most of North America.

In the Southern Hemisphere lie the remaining four biogeographical zones:

- c The Neotropical realm**, which includes

southern Mexico, South and Central America, and the Caribbean;

- d The Ethiopian realm**, which comprises most of Africa, including the island of Madagascar;

- e The Oriental realm**, which covers South and Southeast Asia; and

- f The Australasian realm**, comprising Australia, New Zealand, and New Guinea.

(continued on 7.16)

TRADITIONAL EVIDENCE FOR EVOLUTION 10: BIOGEOGRAPHY (4)

(continued from 7.15)

Evolution of mammals and continental drift

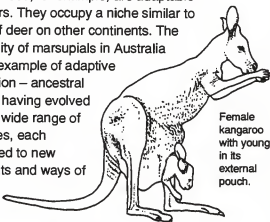
The Northern Hemisphere realms have very similar mammals, but the realms of the Southern Hemisphere have sharply contrasting mammals. In the southern realms, the percentage of endemic species (ones that are found nowhere else) is much higher than in the northern ones. This has since been explained by the movement of continents over millions of years – often referred to as continental drift:

- **The Northern Hemisphere** continents have remained connected by land bridges until recent geological periods, so their mammals have evolved along similar lines, with less time and opportunity for divergence.
- **The Southern Hemisphere** continents have been separated for much longer, so their mammals have evolved along different lines, with more time and opportunity for divergence.

Over two hundred million years ago, the first mammals probably evolved in Asia. From there, they migrated into Africa and Europe and then Australia and the Americas. They traveled over land connections that existed when the present-day continents were merged into one supercontinent called Pangea. Over many millions of years, South America separated from Africa, but Europe, Asia, Africa and, until recently, North America, remained connected by land bridges.

Marsupials Marsupials are mammals whose young develop inside an external pouch. This is in contrast to eutherian (placental) mammals whose young develop inside the uterus. Marsupials only occur in Australia and South America. Elsewhere, they have been replaced by the more successful eutherian mammals. Australian marsupials include the ratlike bandicoot, the kangaroo, and the wombat (a woodchucklike animal). The only eutherian mammals in Australia are those that have been introduced by humans: rabbits, horses, sheep, cattle, and the doglike dingos, for example.

Marsupials and adaptive radiation In Australia, marsupials have evolved to occupy the ecological niches filled elsewhere by eutherian mammals. Kangaroos, for example, are adaptable grazers. They occupy a niche similar to that of deer on other continents. The diversity of marsupials in Australia is an example of adaptive radiation – ancestral forms having evolved into a wide range of species, each adapted to new habitats and ways of life.



Female kangaroo with young in its external pouch.

continental drift



200 million years ago



135 million years ago



65 million years ago

TRADITIONAL EVIDENCE FOR EVOLUTION 11: ARTIFICIAL SELECTION

Natural selection is a process by which organisms most suited to their environment become the ones most likely to survive and leave descendants. The British naturalist Charles Darwin (1809–82) saw artificial selection (breeding, for example) as a model for natural selection.

ARTIFICIAL SELECTION OF PIGEONS

By selecting which individuals are to be mated, animal breeders can breed for desired characteristics. In the case of pigeons, a wide variety of body shapes and plumages can be achieved:

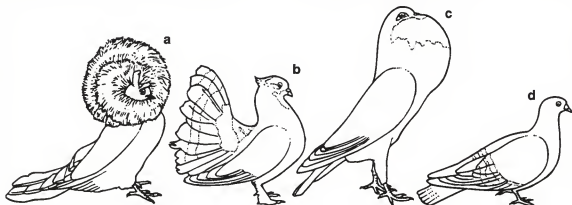
a the jacobin;

b the Indian fantail; and

c the English pouter, for example.

Darwin was convinced that, despite their great differences, all such varieties of pigeon were descended from the wild rock pigeon

(*Columbia livia*) (d) and had acquired their striking forms through selective breeding for desired traits. He argued that if such features could be selected artificially, then, in a similar way, the struggle for survival in nature could weed out individuals less suited to an environment than others. In other words, while humans selectively breed animals for certain features that are considered attractive, nature can “select” for characteristics that aid survival in a particular environment.



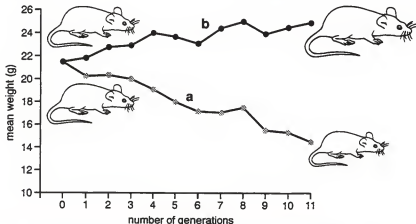
RATE OF DIVERGENCE

Divergent evolution occurs when an original population forms two or more descendent populations, which become increasingly distinct. When subjected to artificial selection, populations can diverge rapidly. In the 1950s, Douglas Scott Falconer (born 1913) kept two populations of mice under identical conditions in all respects but one:

a In one population, he weeded out the largest mice in each generation.

b In the other population, he removed the smallest mice from each generation.

The two populations diverged rapidly in terms of weight. Within 12 generations, the mice in one population (a) averaged about half the weight of those in the other population (b).

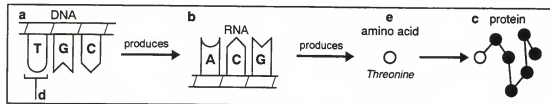


MODERN EVIDENCE FOR EVOLUTION 1: MOLECULAR BIOLOGY (1)

The coming together of biochemistry and genetics in the 1950s created a new discipline – molecular biology. This field has provided new ways of studying evolution.

EVOLUTION OF MACROMOLECULES

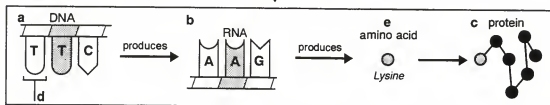
- The structure of macromolecules (larger molecules) such as DNA (deoxyribonucleic acid) (a), RNA (ribonucleic acid) (b), and proteins (c) can be compared between different groups of organisms.
- Evolutionary change appears to take place by the occasional substitution of one building block for another: nucleotides (d) are the building blocks of DNA and RNA; amino acids (e) are the building blocks of proteins.



Key:

 Altered building block

EVOLUTION OVER TIME






- The differences in amino acid sequence between one organism and another are caused by slight differences in the nucleotide sequence of the DNA that codes for the production of that protein.
- The number of differences shows to what degree the two organisms are related.
- The fewer the differences between the same protein in two organisms, the more closely related the organisms are.

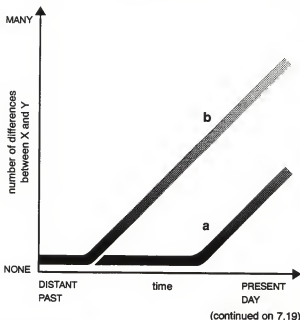
Molecular clocks

Such differences are interpreted as if the molecules are acting as "molecular clocks" that "tick" over millions of years:

- The fewer the differences between the same protein in two organisms (X and Y), then the more recently they are thought to have diverged (took separate evolutionary paths) from a common ancestor.
- The greater the differences between the same protein in X and Y, then the longer ago they diverged from a common ancestor.

Key:

-  X and Y are distantly related
-  X and Y are more closely related
-  Divergent evolution



(continued on 7.19)

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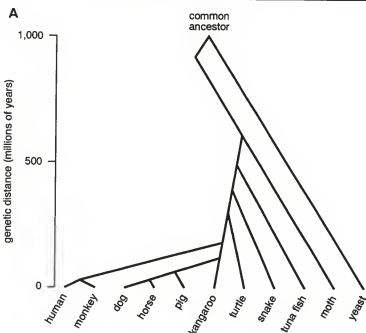
MODERN EVIDENCE FOR EVOLUTION 2: MOLECULAR BIOLOGY (2)

(continued from 7.18)

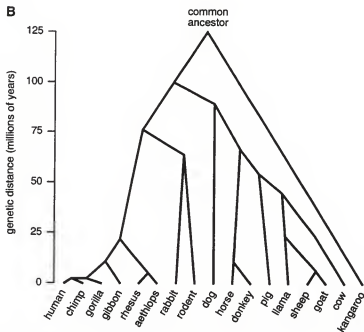
- Some molecular clocks tick relatively quickly, changing over a few million years.
- Others are slow-ticking clocks that change over hundreds of millions of years.

- By choosing a molecular clock of the right speed, the degree of similarity between closely-related or distantly-related forms can be explored.

A If a slow-ticking molecular clock is chosen, the evolutionary relationships between distantly related organisms can be explored. In this example, the molecular differences in the amino acid sequence of cytochrome *c* (a protein involved in cellular respiration) have been measured among organisms as diverse as yeasts and humans. This measure is called the genetic distance. It can be used to estimate the time since one stock diverged from another. Based on cytochrome *c* data, yeast is thought to have diverged from the branch leading to animals about one billion years ago. The genetic distances between various organisms can be used to construct a phylogenetic (or evolutionary) tree depicting the relationships between them.



B If a fast-ticking molecular clock is chosen, the evolutionary relationships between reasonably closely-related organisms can be explored. In this example, the amino acid sequences of several fast-evolving proteins found in mammals have been determined and compared.



Comparing the overall structures of very different organisms reveals little information about when they diverged from a common ancestor. Comparing their molecular similarities and differences, however, can do so. In this way, molecular biology can be used to explore evolutionary relationships when conventional methods are of little use.

MODERN EVIDENCE FOR EVOLUTION 3: MOLECULAR BIOLOGY (3)

As well as testing conclusions drawn from other methods, the techniques of molecular biology have also yielded new insights of their own.

Comparison of RNA sequences in different bacterial forms suggests that bacteria fall into two distinct groups that diverged early on. New techniques such as PCR (the polymerase chain reaction) (see 6.40) amplify trace amounts of DNA for testing. PCR has enabled the DNA from 25-million-year-old fossilized insects found in amber to be compared with that of living relatives.

DNA HYBRIDIZATION

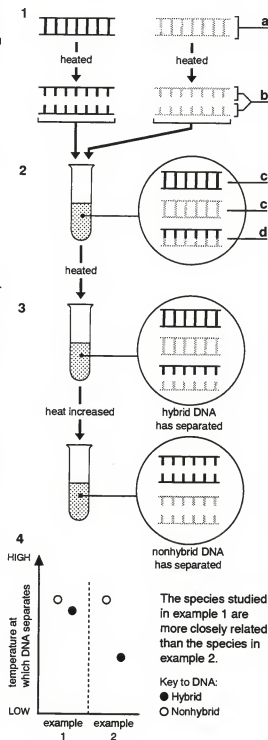
Comparison of the DNA sequences of two present-day organisms is usually carried out by DNA hybridization.

- 1 DNA (a) from two species is separated into its two component strands (b) by heating.
- 2 The single strands from the two species are mixed together. The strands join up:
 - sometimes (c) with a complementary strand from the same species and
 - sometimes (d) with a complementary strand from the other species. This is the hybrid DNA.
- 3 When the mixture is heated, the DNA separates into two strands. The ease with which this happens depends on how closely-matched the two complementary DNA strands are: the hybrid DNA strands separate at a lower temperature than same-species (nonhybrid) DNA. This is because the hydrogen bonding holding the strands together in hybrid DNA is weaker than in nonhybrid DNA as the bases do not all pair up exactly. The poorer the match, the weaker the bonds and, therefore, the lower the temperature of separation.
- 4 The degree of similarity between the two species can be measured by comparing the temperature at which the hybrid DNA separates to the temperature at which the nonhybrid DNA separates. The more closely related the two species are, the smaller the difference in temperatures.

Such comparisons can be charted and estimates made as to when the different species diverged from a common ancestor. For example, recent comparisons of DNA sequences from humans and other primates supports the view that humans are more closely related to chimpanzees than orangutans.

Key:

||||| DNA from organism X
||||| DNA from organism Y



MODERN EVIDENCE FOR EVOLUTION 4: NATURAL SELECTION IN ACTION (1)

Natural selection is a process by which organisms most suited to their environment become the ones most likely to survive and leave descendants.

PEPPERED MOTHS

A classic example of natural selection in action is the case of the peppered moth, *Biston betularia*, which is widespread in Britain. Two forms of peppered moth are commonly found:

a a light form (*typica*), and

b a dark form (called *melanic* or *carbonaria*).

In nineteenth-century Britain, butterfly and moth collecting was a popular pastime. The first reports of the melanic form of the moth were made in 1848 near Manchester, England. Over the next century, the occurrence of the dark form appeared to increase in many parts of Britain. The reason for this was not known, however, until the 1950s work of British biologist Henry Bernard Kettlewell (1907–79).

**Kettlewell's work**

Kettlewell's research showed that, generally:

- the dark form was most abundant in industrial areas, and
- the light form was most abundant in rural areas.

Key:



Proportion of light to dark moths

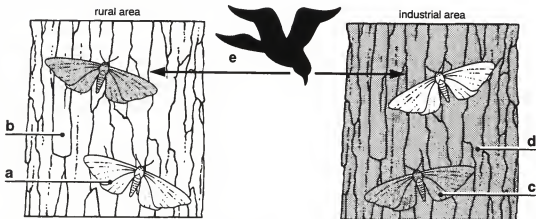


MODERN EVIDENCE FOR EVOLUTION 5: NATURAL SELECTION IN ACTION (2)

(continued from 7.21)

The relative abundance of the two forms of moth could be explained by the habitats in which they lived:

- light moths (a) were well camouflaged against the pale background of rural trees (b); and
- dark moths (c) were better camouflaged against the dark background of the soot-covered trees (d) found in industrial areas.



As peppered moths are preyed upon by birds:

- in rural areas, the dark moths were more visible and more likely to be eaten by birds (e); but
- in industrial areas, the light moths were more visible and more likely to be eaten.

Using mark-and-recapture experiments and by observing bird predation, Kettlewell showed that this selective predation could largely account for the observed distribution of forms:

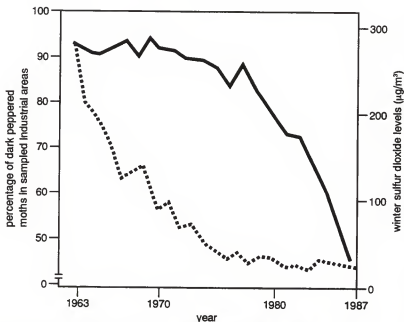
- as light moths were more likely to survive and leave descendants in rural areas; but
- dark moths were more likely to survive and leave descendants in industrial areas.

The changing frequencies of the colored forms of this moth is one of the clearest and best documented examples of natural selection occurring in the wild.

Further proof of Kettlewell's findings came in later years. In 1956, the Clean Air Act was introduced. It drastically reduced sooty air pollution in Britain. As might be expected, the dark form of the moth gradually declined in many industrial areas.

Key:

- Frequency of moths
- Sulfur dioxide levels (closely related to levels of soot)



MODERN EVIDENCE FOR EVOLUTION 6: NATURAL SELECTION IN ACTION (3)

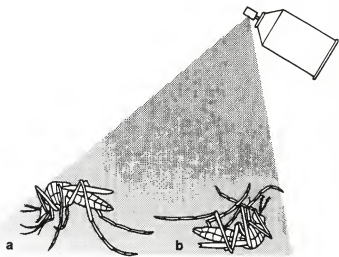
Many of the best demonstrations of natural selection are those that involve some environmental change caused by human intervention.

DDT RESISTANCE

Since World War II (1939–45), the widespread use of the insecticide DDT (dichlorodiphenyltrichloroethane) has led to the rapid evolution of DDT-resistance in many populations of flies and mosquitoes:

- a** those insects that are naturally DDT-resistant survive, while
- b** those that are not are killed.

As a result, the insect population comes to contain DDT-resistant individuals that interbreed and pass on their genetic traits for DDT-resistance.

**Mechanisms of DDT resistance**

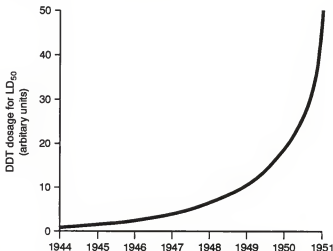
Different genes may confer different forms of resistance. The individuals in surviving populations become resistant to DDT in a variety of ways. House flies and fruit flies, for example, have been shown to use several mechanisms to combat the toxicity of DDT. These mechanisms involve genes on several chromosomes that encode for a variety of effects, including:

- enzymes (biological catalysts) that break down DDT into less toxic products;

- increasing the lipid (fat) content of the body tissues so that fat-soluble DDT is separated out from other body tissues where it could exert a harmful effect;
- a reduced response by the nervous system to the toxic effects of DDT;
- a reduction in the insect's capacity to absorb DDT; and
- a behavioral response that reduces contact with DDT.

Spread of resistance

In a 1940s–50s survey of Illinois farms, the lethal dose of DDT necessary to kill 50% of individuals (called the LD_{50}) rose steeply in house flies following several years of DDT spraying by farmers in the region. This example illustrates the speed and extent of resistance development in pest insects.



MODERN EVIDENCE FOR EVOLUTION 7: NATURAL SELECTION IN ACTION (4)

Bacteria multiply very rapidly by binary fission (simple division). They can also transfer genetic material (DNA) from one individual to another in a variety of ways. As a result, bacteria can evolve very rapidly in response to changing environmental conditions. One example of this is the resistance to antibiotics that many bacteria have developed within the last 50 years.

ANTIBIOTIC RESISTANCE AND BACTERIA

Antibiotics are chemicals that kill bacteria or inhibit their growth. They are commonly used to combat bacterial diseases. The indiscriminate and widespread use of antibiotics has led, however, to many bacteria becoming resistant to the effects of these chemicals.

By a combination of natural selection and transformation it is possible for bacterial populations to become resistant to a range of antibiotics.

Natural selection

1 When a bacterial population

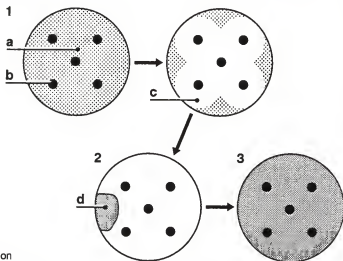
(a) is first exposed to an antibiotic (b), any susceptible bacteria (c) are killed or immobilized.

2 Any resistant bacteria (d) that remain can multiply rapidly because competing individuals are absent.

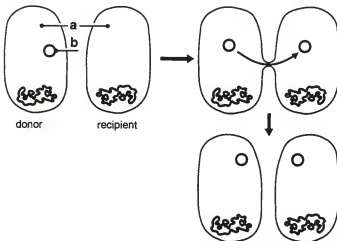
3 Soon, any surviving populations comprise only resistant bacteria.

Key:

 Antibiotic-resistant bacterial population

**Transformation**

Bacteria (a) are able to transfer genetic material from one individual to another via plasmids (circular DNAs separate from the bacterial chromosome) (b). Bacteria that were previously without genes that confer antibiotic resistance can acquire them by receiving a plasmid carrying the genes. These bacteria are said to have been transformed.

**Spread of antibiotic resistance**

Multiple resistance to antibiotics in bacteria has occurred in some hospitals in the United States, Europe, and elsewhere. Current recommended practice is for patients:

- to be prescribed antibiotics only when vital;
- to be given a full but short course; and, if the treatment is unsuccessful,

- to be given another antibiotic, preferably one with a very specific action, that has been held in reserve.

The indiscriminate use of broad-spectrum antibiotics in medicine and in animal feed supplements is being discouraged to reduce the incidence of antibiotic-resistant bacteria.

SOURCES OF GENETIC VARIATION

Natural selection is a process by which organisms most suited to their environment become the ones most likely to survive and leave descendants. Natural selection acting on genetic variation within a population can produce evolutionary change. There are two main sources of genetic variation: mutations and sexual reproduction.

SOURCE OF GENETIC VARIATION	MECHANISMS FOR GENERATING GENETIC VARIATION	NATURE AND RELEVANCE TO NATURAL SELECTION
MUTATIONS <ul style="list-style-type: none"> • Mutations are spontaneous and inheritable changes in the genetic material of a cell. • They are a source of genetic variation for both sexually and asexually reproducing organisms. • There are two types of mutation: gene mutations and chromosome mutations. • These can occur naturally (as mistakes during cell division) or can be caused by mutagens. 	<p>Gene mutations These are small scale changes in the genetic material that alter a single gene. They involve a change in one or more nucleotides (DNA (deoxyribonucleic acid) building blocks – of a gene. New alleles (gene forms) normally arise by gene mutations.</p> <p>Chromosome mutations These are large scale changes in the genetic material that alter the gross</p> <p>structure of a chromosome or change the number of chromosomes in a cell.</p> <p>Mutagens Natural mutation rates tend to be low, but they are increased by external factors called mutagens. Mutagens include various types of radiation – such as nuclear radiation, ultraviolet (UV) light, and X rays – and certain chemicals (for example, the tars found in tobacco smoke).</p>	<ul style="list-style-type: none"> • Mutations create new alleles and large-scale changes in an individual's genome (complete set of genes). • Advantageous mutations occur rarely. Such mutations, however, are the raw material of evolution – they provide the genetic variation on which natural selection can act. • Natural selection weeds out harmful mutations in a population, and keeps these at a low level; it also ensures that beneficial mutations may spread rapidly through a population.
SEXUAL REPRODUCTION <ul style="list-style-type: none"> • This is an important source of genetic variation for most species. • In sexually-reproducing eukaryotic organisms (such as many plants and animals) the variation is generated in three ways: independent assortment; crossover; and random fertilization. 	<p>Independent assortment • Meiosis is the cell division that produces gametes (sex cells) such as ova (eggs) and sperm.</p> <p>• Chromosomes generally fall into homologous (matching) pairs – one chromosome of which is derived from the mother and the other from the father.</p> <p>• During meiosis, homologous chromosomes align at random along the equator of the cell.</p> <p>• Which chromosome of a homologous pair migrates to which pole of the cell – and hence which daughter cell – occurs at random.</p> <p>• This is called independent assortment. It ensures that the chromosomes in a gamete are a random mix of paternal and maternal chromosomes.</p> <p>Crossover During meiosis, homologous chromosomes might exchange corresponding lengths of DNA – the genetic material. This is called crossover. It is a mechanism that alters the combination of alleles on a single chromosome.</p> <p>Random fertilization Which male gamete (and its particular combination of alleles) combines with which female gamete (and its particular combination of alleles) is a random process. The number of possible combinations is so large as to be almost infinite.</p>	<ul style="list-style-type: none"> • The mechanisms of sexual reproduction generate new combinations of alleles by shuffling existing genetic material. • New combinations of alleles and interactions between the alleles may be advantageous to the offspring and increase their chances of survival.

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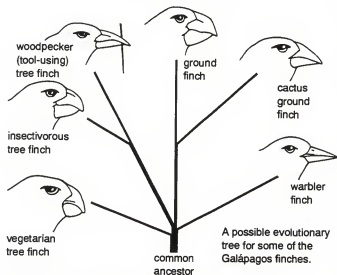
MACROEVOLUTION AND MICROEVOLUTION

By the 1930s, with the integration of Mendelian genetics and Darwinian evolutionary theory, a new mathematical approach to the study of evolution was being developed by researchers such as Sewall Wright (1889–1988) in the United States and Ronald Fisher (1890–1962) and J. B. S. (John Burdon Sanderson) Haldane (1892–1964) in the United Kingdom. This approach is called population genetics. It involves examining changes in characteristics within populations using statistical methods.

With the establishment of population genetics, the study of evolution gradually came to be divided into two levels of focus: microevolution and macroevolution.

MICROEVOLUTION

- This relates to evolution within populations – the kind of small-scale evolution studied by population geneticists.
- One of the main focuses of this work is in exploring speciation (how new species arise).
- Evidence suggests that the six main groups of Galápagos finches (see 7.13), comprising 13 species, have evolved from a single ancestral form.



MACROEVOLUTION

- This refers to evolution on a grander scale. It encompasses the evolution of larger divisions than species – genera, families, orders, classes, and so on right up to kingdoms.
- Macroevolution uses many of the tools of traditional evolutionary investigation – comparative anatomy, embryology, and the fossil record, for example – supplemented by newer techniques such as comparative molecular biology.

Macroevolution is currently focusing on issues such as:

- major evolutionary trends within plant and animal groups;
- how revolutionary new structures and designs arise within evolutionary lineages; and
- mass extinctions.

A possible evolutionary tree for the classes of vertebrates.

Era	Period	Vertebrate group						Years ago (millions)
Cenozoic	Quaternary							2
	Tertiary							63
Mesozoic	Cretaceous							138
	Jurassic							205
	Triassic							240
	Permian							290
	Pennsylvanian							330
Paleozoic	Mississippian							360
	Devonian							410
	Silurian							435
	Ordovician							500
	Cambrian							570

POPULATION GENETICS 1: GENE POOLS

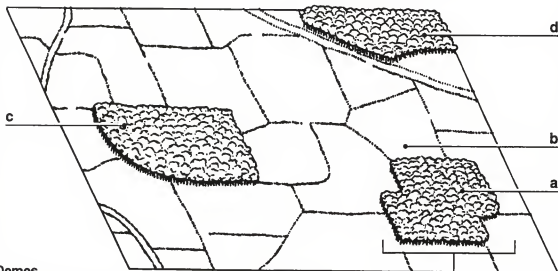
POPULATIONS

A population is a collection of individuals of the same species living in the same place at the same time; for example, the trout population of a particular lake or the rabbit population of a certain hillside.

Interbreeding

- The members of a population are much more likely to interbreed with one another than with individuals of other populations of the same species.

- Although there may be some movement of individuals between populations (migration), a given population will often remain genetically distinct from another population and will perpetuate itself over time by the interbreeding of individuals within it.
- For example, the mice population in a woodland (a) surrounded by agricultural land (b) will most likely remain genetically distinct from other mice populations in other woodland areas (c and d).

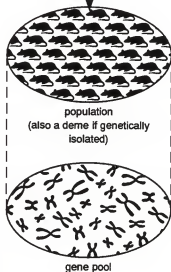


Demes

- Geneticists refer to a population that is, more or less, genetically isolated from other populations as a deme. A deme therefore represents a genetic unit.
- **Gene pools** The genetic make up of a deme, that is the sum total of all the different genes in the population, is called the gene pool.

Gene pools and evolution

- Microevolution occurs at the level of a population, not at the level of the individual. It is populations that undergo evolutionary change, not individuals.
- The evolutionary future of a deme depends on its gene pool.
- By studying how a gene pool changes over time, population geneticists can begin to explore microevolutionary processes.
- **Speciation** When a deme evolves to the point where it can no longer interbreed successfully with other demes of the same original species, even when brought into contact, then the deme has effectively formed a new species. The development of a new species is called speciation. How speciation occurs is one of the major interests of geneticists studying microevolution.






POPULATION GENETICS 2: ALLELIC FREQUENCIES

ALLELES

Genes can occur in different forms called alleles. The alleles of a gene code for the same trait but not necessarily for the same expression of that trait. For example, the fruit fly gene for wing shape (*Vg*) has two alleles: *Vg* (normal wings) and *vg* (vestigial, or miniature, wings).

Allelic frequencies

- The occurrence of an allele in a population relative to all the other alleles of the same gene is known as its allelic frequency.
- Allelic frequencies are a way of measuring genetic variation within a population.
- Diploid organisms – such as fruit flies – have two copies of each gene. In a hypothetical population of 100 fruit flies, for example, there will be 200 alleles that code for normal or vestigial wing shape within the population.
- At this gene locus (location), a given individual may have two alleles that are identical or two alleles that are different. In fruit flies, for example, are three possible genotypes (genetic constitutions) comprising either identical or different alleles: *Vg/Vg*; *Vg/vg*; or *vg/vg*.
- In the example below: the allele *Vg* occurs 150 (112 + 38) times out of a possible 200 occurrences; *vg* occurs 50 (38 + 12) times out of 200. These proportions are the allelic frequencies of *Vg* and *vg*.
- Allelic frequencies can be expressed either as proportions or percentages: 0.75 or 75% in the case of *Vg*; or 0.25 or 25% in the case of *vg*. The combined frequencies of *Vg* and *vg* must equal 1.00 or 100%.

				TOTALS
Genotype	<i>Vg/Vg</i>	<i>Vg/vg</i>	<i>vg/vg</i>	
Phenotype	normal wings	normal wings	vestigial wings	
Number of Individuals	56	38	6	100
Number of alleles	<i>Vg</i> 112 <i>vg</i> –	38 38	– 12	150 50 200
Allelic frequencies	$\left. \begin{aligned} Vg &= \frac{150}{200} = 0.75 \text{ (or 75\%)} \\ vg &= \frac{50}{200} = 0.25 \text{ (or 25\%)} \end{aligned} \right\}$			100% (or 1.00)

Polymorphic genes

- If the most common allele occurs at a frequency of less than 0.99 (99%), the gene is said to be polymorphic – it has more than one form that occurs a significant number of times.
- If the most common allele occurs at a frequency of 0.99 (99%) or more, then the gene is monomorphic – it has only one form that occurs a significant number of times.

Polymorphism

Polymorphism means the existence of many different forms. In genetics, it refers to the occurrence of different alleles of a gene within a population. For example, the occurrence of normal wings and vestigial wings in fruit flies is caused by the existence of more than one form of the gene at that locus. The existence of different forms of the fruit fly wing is therefore an example of a polymorphism.

POPULATION GENETICS 3: HARDY-WEINBERG PRINCIPLE (1)

- Does the process of sexual reproduction change allelic frequencies within a population? Put another way, does the normal mechanism of inheritance itself produce evolutionary change?

In 1908, the English mathematician Godfrey Harold Hardy (1877–1947) and the German

physician Wilhelm Weinberg (1862–1937) independently showed that in an idealized population which conformed to certain criteria, evolutionary change would not result from normal reproductive processes. This principle is called the Hardy-Weinberg principle or the Hardy-Weinberg law.

The Hardy-Weinberg principle can be summarized in three main statements. In an idealized population:

- The frequencies of genotypes are a simple function of the frequencies of their alleles (called the binomial function).
- No matter what the genotypic frequencies are initially, they will come to fit the Hardy-

Weinberg equilibrium in the next and in subsequent generations as long as the idealized conditions are maintained.

- The processes of sexual reproduction do not, in themselves, change the frequencies of alleles or genotypes from one generation to the next once equilibrium is achieved.

Demonstration of the Hardy-Weinberg principle

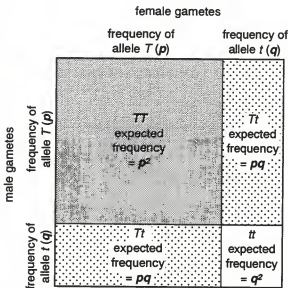
A single gene in an idealized human population is being considered. There are just two alleles of this gene: T and t . T is dominant – expressed in preference to the recessive (“weaker”) allele t . The phenotype (expression) of this gene is the ability to taste a chemical compound called PTC (phenylthiocarbamide).

Genotypes and alleles Individuals in the population have one of three genotypes: TT , Tt , or tt . Those with the genotypes TT and Tt have the dominant phenotype – they can taste PTC. Those with the genotype tt have the recessive phenotype – they cannot taste PTC.

If:

- p is the frequency of allele T , and
- q is the frequency of allele t ,
- then the three genotypes: TT , Tt , and tt will be produced in the proportions of p^2 , $2pq$, and q^2 respectively.

This is a natural consequence of the random fertilization of gametes (sex cells), such as ova (eggs) and sperm in humans. In all subsequent generations, these proportions will be maintained as long as idealized conditions remain. A population is said to be in Hardy-Weinberg equilibrium when its genotypes occur in these proportions.



According to the Hardy-Weinberg principle, the distribution of alleles T and t among genotypes TT , Tt , and tt is expected to be:

$$TT : Tt : tt$$

$$p^2 : 2pq : q^2$$


where p = frequency of allele T

where q = frequency of allele t

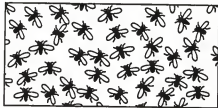
note: $p + q = 1$

POPULATION GENETICS 4: HARDY-WEINBERG PRINCIPLE (2)

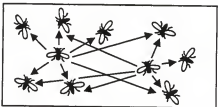
- What are the idealized conditions in which the Hardy-Weinberg principle applies?
A population will be in Hardy-Weinberg equilibrium as long as the following conditions hold:

The population is large

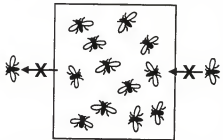
The smaller the population, the greater the likelihood that chance variations will alter expected allelic and genotypic frequencies.

**Mating is random**

Individuals within the population mate at random with respect to the gene under consideration.

**There is no emigration or immigration**

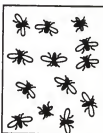
If migration into or out of the population is significant and if it takes place between neighboring populations that have different allelic and genotypic frequencies, then this will cause deviations from expected frequencies. In practice, migration is often negligible for many populations, but for some it has a major impact.

**Natural selection is not operating on the gene**

If one allele is associated with a higher probability of survival and, therefore, reproductive success, then genotypic and allelic frequencies will gradually change accordingly. For example, as vestigial-winged fruit flies are usually at a disadvantage compared to normal-winged fruit flies, the normal-winged form tends to predominate.



natural selection
not operating



natural selection
in action

There is no mutation

In reality, mutation rates in natural populations are sufficiently low not to affect expected frequencies significantly.

If a population is not in Hardy-Weinberg equilibrium

In practice, deviations from frequencies predicted by the Hardy-Weinberg principle are used as evidence that one or more of the above criteria does not apply. For example, there could be:

- inbreeding due to small population size;
- nonrandom mating;

- migration; and/or
 - natural selection may be operating on the particular gene within the population.
- Assessing whether or not a population is in Hardy-Weinberg equilibrium is, therefore, a very useful tool in exploring evolutionary change within populations.

VARIABILITY IN NATURAL POPULATIONS

Genetic variation is the raw material on which natural selection can act.

- **Genetic variation** is generated in most eukaryotes (such as plants and animals) by mutation coupled with the processes of sexual reproduction.
- **Natural selection** is a process by which organisms most suited to their environment become the ones most likely to survive and leave descendants.

But once this genetic variation is produced, how is it maintained within populations? Surely as individuals in a population adapt to their surroundings, they will become more and more alike genetically? The more successful characteristics and the alleles (gene forms) that produce them will be retained and the less successful ones will be removed by natural selection?

LEVELS OF GENETIC VARIATION

With the introduction of biochemical techniques to study natural variation in populations in the 1960s, it was soon discovered that there was far greater variation within natural populations than previously suspected. Electrophoresis has been used to examine genetic variation in proteins. This technique is able to distinguish different forms (allozymes) of the same enzyme (biological catalyst). By the late 1970s, it was estimated that over 40% of the 10,000 or so genes in fruit

flies are polymorphic (each has more than one form that occurs a significant number of times). Each polymorphic gene has between two and six possible alleles and these exist at sufficiently high frequencies to suggest that the average fruit fly is heterozygous (has nonmatching alleles) for about 14% of its genes. Similarly high levels of genetic variation have been found in many different plant and animal species.

Organisms	Mean percentage of polymorphic genes	Mean percentage of heterozygous alleles per individual
Amphibians	27	8
Birds	15	5
Fish	15	5
Flowering plants	46	17
Fruit flies	43	14
Land snails	44	15
Large mammals	23	4
Marine snails	17	8
Reptiles	22	5
Rodents	20	5
Social bees and wasps	24	6

This table gives estimates of genetic variation in natural populations based on analysis of protein variation by electrophoresis.

Maintaining levels of genetic variation

Several processes are thought to retain high levels of genetic variation within populations:

- **Natural selection** is one of these processes. It is very likely, however, that many detectable variants are neither beneficial nor harmful – they are neutral, and will therefore not be selected for or against.
- **Gene flow** into the population – by immigration of individuals from genetically different populations and by outbreeding

with individuals from other populations – can also increase levels of genetic variation.

- **Neutralist theory** According to this theory, random processes such as genetic drift (see 7.32) and gene flow, rather than natural selection, account for much of the observed levels of genetic variation.
- On balance, it is likely that a combination of random processes and natural selection accounts for observed levels of variability.

GENETIC DRIFT

● **Genetic drift** refers to changes in allelic frequencies that happen by chance rather than by natural selection (a process by which organisms most suited to their environment become the ones most likely to survive and leave descendants).

● **Allelic frequencies** The proportion of an allele (gene form) in a population relative to all the other alleles of the same gene is known as its allelic frequency.

GENETIC DRIFT AND EVOLUTION

Genetic drift could be an important mechanism of evolutionary change in small or isolated populations. For example:

- If a population of 100 individuals contains an allele at, for example, 1%, on average one or two members will have that allele.
- If these individuals were to die by accident before they had a chance to breed, that

allele would be lost from the population.

- If the population contained 10,000 individuals, however, many more members (100 to 200) would carry the rare allele and the possibility of it disappearing by chance events alone would be much less.

So, the loss of rare alleles is likely to have more impact on small than large populations.

Cheetah populations and genetic drift

It appears that present-day cheetah populations contain relatively little genetic variation. Geneticists suspect that the cheetah nearly died out 10–12,000 years ago (toward the end of the last Ice Age) and that the modern animals are descended from just a few surviving individuals. This has created three major problems:

- Existing populations have little genetic variation to cope with environmental change.
- The originally small population size has led to inbreeding, with some loss of fertility.
- Harmful recessive alleles are more likely to be combined in inbred offspring.

Attempts to boost natural cheetah populations by captive breeding have had little success.

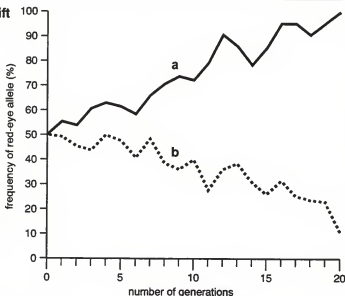
Fruit fly populations and genetic drift

Genetic drift can cause an allele to drift to a higher frequency simply by chance. In one laboratory study of fruit flies, two small populations were set up. Each had allelic frequencies of 50% for the red-eye allele and 50% for the brown-eye allele. Within 20 generations:

a In this population, the red-eye allele was the only one remaining – it had drifted to an allelic frequency of 100%.

b In this population, the red-eye allele had drifted to a frequency of 10%.

These differences were attributed to chance matings and deaths.



The founder effect

When a few individuals become separated from their parent population, they form a gene pool that is likely to be genetically different from the parent population as it is much smaller. Genetic drift could cause this founder population to become even more different

from the parent population. This probably occurs when islands are colonized. In such cases, genetic drift may contribute significantly to the process of speciation (the evolution of new species). An example of this is the case of the Galápagos Island finches (see 7.13).

GENE FLOW

The movement of alleles (gene forms) from one population to another is called gene flow.

- **In animal populations**, gene flow commonly occurs by immigration or emigration followed by interbreeding.
- **In flowering plants**, wind or other means of dispersal can scatter seeds or pollen grains far beyond the area of local populations.
- **The extent of gene flow** between two populations depends on how close they are geographically and the ease with which individuals or their gametes (sex cells) — such as pollen grains — can pass between the populations.

Gene flow maintains the genetic integrity of species:

- Populations of the same species can interbreed. They therefore share a common gene pool, because alleles are exchanged between populations that interbreed.
- If gene flow is interrupted for many generations, some populations might diverge from the original common gene pool and could even form new species.

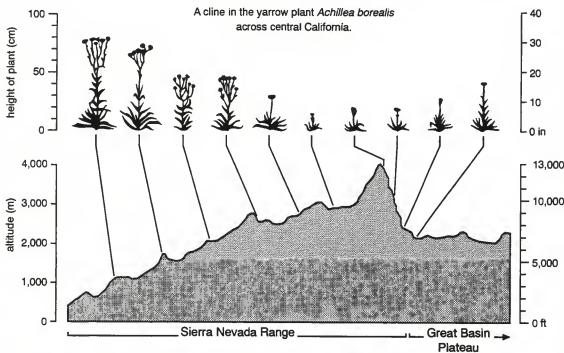
GENE FLOW AND NATURAL SELECTION

Natural selection is a process by which organisms most suited to their environment become the ones most likely to survive and leave descendants.

- Gene flow between populations tends to increase their genetic similarity.
 - Natural selection commonly has the reverse effect: it tends to make every population uniquely adapted to its particular habitat.
- One possible outcome of these two conflicting forces is a gradation of genetic variation along a large-scale environmental feature. The existence of gradation of inherited characteristics along an environmental gradient is called a cline.

Example of a cline

In a 1940s study of the yarrow plant *Achillea borealis*, a transect across central California showed that adjacent populations differed in characteristics such as rate of growth, maximum height, leaf shape, and growing season. These characteristics were shown to be genetically controlled, because when samples were grown under the same conditions, the plants still differed in these and other respects. High-altitude forms grew poorly under low-altitude conditions and vice versa, for example. Adjacent populations showed gradation in characteristics, suggesting gene flow between them.



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STABILIZING SELECTION

NATURAL SELECTION

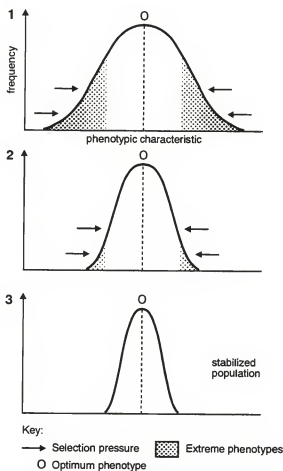
This is a process by which organisms most suited to their environment become the ones most likely to survive and leave descendants. Natural selection is responsible for maintaining a relatively constant genetic constitution for a species as well as causing it to change.

Stabilizing selection

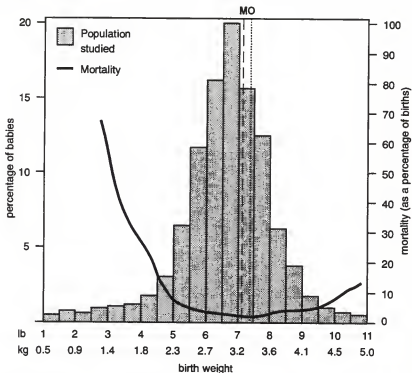
Natural selection that maintains a high incidence of optimal (most successful) forms in a population is called stabilizing selection. It occurs in all populations, but is particularly apparent when an environment stays reasonably constant over time. In such cases, natural selection:

- tends to eliminate extreme forms from the population (1 to 2), and
- results in an optimum phenotype (such as birth weight) that is close to the mean value of the characteristic for that population (3).

In this way, stabilizing selection tends to promote the best fit of a population to its stable environment.



A classic example of this effect was described by the British biologists M. N. Karn (1898–1972) and Lionel Penrose in the 1940s. There is a close relationship between birth weight and mortality for human babies. The optimum survival weight (O) was very close to the mean birth weight (M) for the population they studied. Mortality is much higher at extremely high and low birth weights.

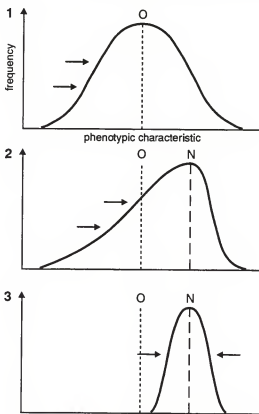


DIRECTIONAL SELECTION

Directional selection operates in response to gradually changing environmental conditions. It favors one extreme of the range of an inherited characteristic at the expense of the other extreme. It causes the most abundant phenotype (such as moth body color) in a population to shift from the originally most-favored phenotype (such as light body color) (1) to a new phenotype (such as dark body color) (2) at one extreme of that characteristic. Once the shift occurs, stabilizing selection (see 7.34) predominates and creates a new distribution tightly clustered around the new optimum phenotype (3).

Examples of directional selection

Classic examples of directional selection in the wild often involve some form of human influence on the environment. The increase in abundance of dark forms of the peppered moth in industrial areas, and increase in abundance of light forms in rural areas (see 7.21), are examples of directional selection. The development of populations of metal-tolerant plants on mining slag heaps is another example.



Key:

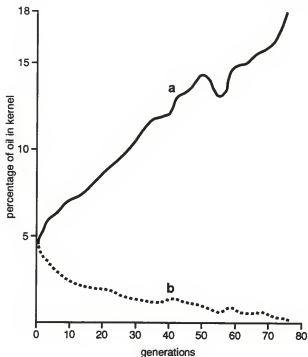
- Main selection pressure
- O Original optimum phenotype
- N New optimum phenotype

Directional selection and evolution

This type of selection brings about evolutionary change by providing a selection pressure that encourages the increase in frequency of new or comparatively uncommon alleles (gene forms) within a population. Directional selection forms the basis for much artificial selection by animal and plant breeders, who select for extreme traits such as highest meat yield, tallest plants, largest blooms, and so on.

At the University of Illinois, selection for high and low oil content in corn kernels over a period of roughly 70 years has produced two populations:

- a One with a high content, that is further increased by selective breeding.
- b The other population now has a negligible oil yield.



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DISRUPTIVE SELECTION

Disruptive selection favors two extremes of a phenotypic distribution, with selection occurring against the mean phenotype or intermediate form (1 and 2). Eventually this gives rise to a bimodal distribution (3) in which two distinct forms predominate.

EXAMPLES OF DISRUPTIVE SELECTION

Disruptive selection is a relatively rare form of selection. Nevertheless, it is important in circumstances where a diverse habitat is occupied and the two forms are adapted to different parts of that environment. Two of the few well-documented examples are found in swallowtail butterflies.

Papilio machaon

In the European swallowtail butterfly, *Papilio machaon*, two forms of the butterfly are found in some localities. Each form is adapted to the different color of the plants on which they lay their eggs:

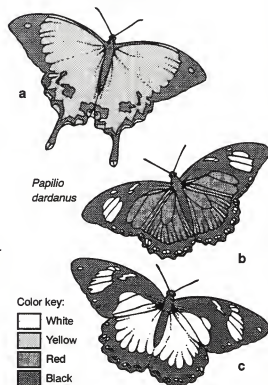
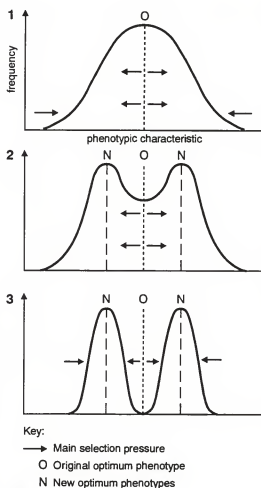
- One form tends to lay eggs on leaves or stems that are brown and the caterpillars give rise to pupae (pre-adult forms) that are also brown.
- Another form tends to lay its eggs on green leaves and stems and the pupae in this case are also green.

The color differences seem to be inherited (genetically determined), and there are very few forms that are intermediate in color.

Papilio dardanus

One species of African swallowtail butterfly, *Papilio dardanus*, is a remarkable product of disruptive selection. The males of the species (a) are all similar in color, but the females exist in two radically different colors:

- One form (b) is white, black, and red. It closely resembles the females of a poisonous species, *Danaus chrysippus*.
- The other form (c) is white and black. It closely mimics the appearance of the females of another poisonous species of butterfly, *Amaurus niavius*. By mimicking the appearance of poisonous butterflies, the females are less likely to be eaten by potential predators that have learned to avoid the poisonous forms. By mimicking two different forms, the females have a greater chance of avoiding predation.



WHAT IS A SPECIES?

For sexually reproducing organisms, a species is traditionally defined as a group of individuals capable of interbreeding to produce fertile offspring.

- The members of a species share a large number of features in common: structural, physiological, biochemical, and behavioral features, for example.
- The individuals of a species form a common gene pool separate from other species.
- There is little or no gene flow (movement of genes) between two species.
- Closely related species may look similar, but they cannot interbreed with one another to produce fertile offspring. For example, a horse and an ass can interbreed but the resulting offspring are infertile hybrids: mules (if the male parent is an ass) or hinnies (if the female parent is an ass).

By definition, two species are distinct because they are unable to breed with each other to produce fertile offspring. In practice, however, this distinction is not always clear cut.

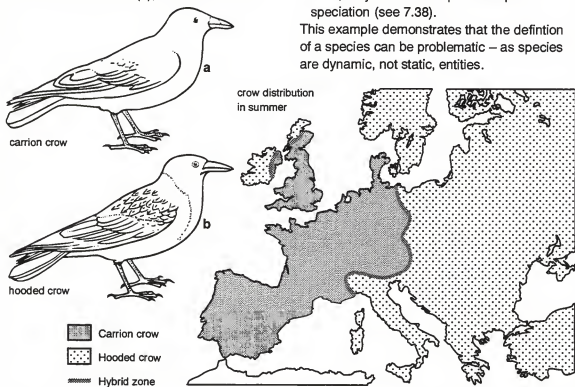
Plants The genetic systems of plants are more adaptable, and two existing species have, in a few instances, interbred to produce a new species. For example, the British small cord grass, *Spartina maritima*, and American cord grass, *Spartina alterniflora*, have interbred to produce a new species called *Spartina anglica*, which is unable to breed with its ancestral species but is self-fertile. The evolution of a new species is called speciation.

Animals In western Europe are found two closely related species of crow: the carrion crow, *Corvus corone* (a), and the hooded

crow, *Corvus cornix* (b). Hybrids between the two are found in a zone up to 10-kilometers (6-miles) wide that separates the two species in summer. These hybrids appear to have reduced fertility compared to the parent species. Nevertheless, some intermingling of the two gene pools is taking place.

- It is possible that the crows are still on the way to becoming two separate species – in which case, they are an example of sympatric speciation (see 7.39).
- Alternatively, the two species may have evolved in geographic isolation and then come together at a later date – in which case, they are an example of allopatric speciation (see 7.38).

This example demonstrates that the definition of a species can be problematical – as species are dynamic, not static, entities.



ALLOPATRIC SPECIATION

Speciation is the evolution of new species. Allopatric speciation refers to the evolution of two or more species from an ancestral species as a result of geographical separation:

- The ancestral gene pool becomes split into two or more gene pools that are no longer connected by gene flow (the movement of genes between populations).
- The resulting gene pools diverge from one another to establish new species.
- Over many generations, the new forms become sufficiently distinct that were they to be brought together with each other, or the original parental population, they would be unable to interbreed successfully.

THE FOUNDER EFFECT

Allopatric speciation is much more likely to occur if one or more of the descendent gene pools is fairly small. In a small gene pool, genetic drift (the loss of genes by chance deaths, for example) is likely to be significant. As a result, a genetically distinct population might be produced even before selection pressures result in adaptive change in the population. This is called the founder effect.

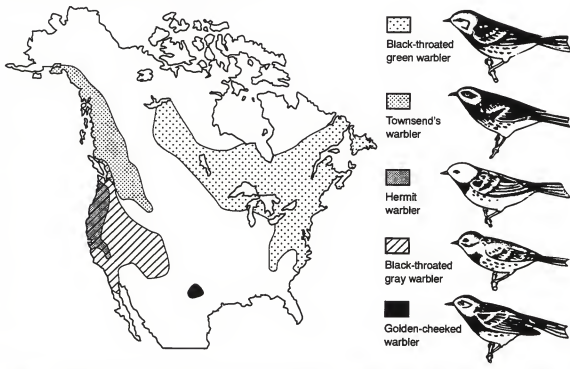
On islands

The evolution of Galápagos Island finches (see 7.13) from an ancestral, mainland form is, perhaps, the classic example of allopatric speciation in oceanic islands.

On continents

Allopatric speciation can also occur on continents. The ancestral species of North

American wood warblers were split into genetically distinct gene pools on a number of occasions over the last million years. During that time at least four major glaciations (Ice Ages) covered much of Canada, the northern United States, and the western mountains with thick ice. The normally widely-distributed wood warblers were pushed back into isolated pockets. In some cases, the separated populations evolved to become distinct species. When thawing subsequently occurred, and populations reestablished contact, some had developed sufficient genetic differences to be unable to interbreed. Evidence suggests that five species of present-day North American wood warbler evolved from one ancestral form in this way.



SYMPATRIC SPECIATION

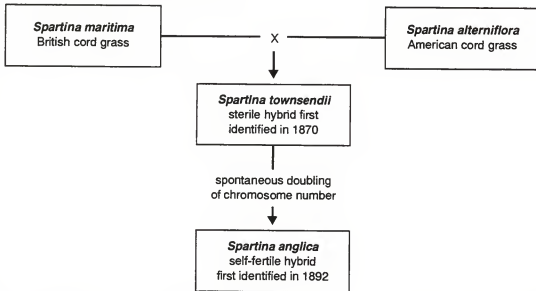
Speciation is the evolution of a new species. Sympatric speciation refers to the evolution of two or more species from an ancestral species in the same place at the same time:

- It requires the development of some form of reproductive isolating mechanism in a population within a specific locality.
- This mechanism may be structural, physiological, behavioral, or genetic. It serves to split the population into two or more separate gene pools.

Sympatric speciation in plants

In plants, sympatric speciation has been established for the fertile hybrid of the British small cord grass, *Spartina maritima*, and American cord grass, *Spartina alterniflora*. In nineteenth-century England, cross-breeding between these two forms took place in the wild. The resulting sterile hybrid, *Spartina*

townsendii, underwent doubling of its chromosome number and became self-fertile but was unable to interbreed with its parental species. A new species had been formed, *Spartina anglica*, which has since spread to inhabit many English estuaries.

**Sympatric speciation in animals**

No absolutely convincing example of sympatric speciation in animal species in the wild has yet been demonstrated. Sympatric speciation does, however, provide an explanatory mechanism of how closely related species that probably arose from a common ancestor by temporary geographic isolation can now coexist within the same locality. For example:

- On the Galápagos Islands the finch *Camarhynchus pauper* is found on only one island where it coexists with a related form *Camarhynchus psittacula*.
- The second species is found on several other Galápagos islands.
- Where the two species coexist, they have

undergone directional selection (see 7.35) so that their beak sizes are now different.

- Not only do the two species feed on different food items, but beak size is used to discriminate between one species and the other when individuals choose mates.
- This isolating mechanism has structural (beak size) and behavioral (diet) components. It ensures that the two species can coexist without interbreeding.
- On islands where *Camarhynchus pauper* is absent, *Camarhynchus psittacula* has not been subjected to strong directional selection for beak size and it has a smaller beak, much closer in size to that of *Camarhynchus pauper*.

HETEROZYGOTE ADVANTAGE

The Hardy-Weinberg principle (see 7.29) predicts the level of alleles (gene forms) that would be expected in a very large, randomly-mating population free from mutation, migration, and natural selection. Sometimes individuals with heterozygous (nonmatching) alleles are more abundant in the population than the Hardy-Weinberg principle predicts. In some cases, this can be explained by the heterozygous form being more advantageous than either of the homozygous forms. The classic example in humans is the case of sickle-cell anemia.

SICKLE-CELL ANEMIA

This disease is caused by a recessive allele (Hb^S) that has the tendency to make normal red blood cells distort into the characteristic sickle shape when blood oxygen levels are low. The damaged red blood cells reduce the blood's oxygen-carrying capacity and may block small blood vessels and impede circulation. This leaves the sufferer with anemia and symptoms such as extreme tiredness, headaches, and muscle cramps. Over time, the condition limits growth and might even cause kidney or heart failure.

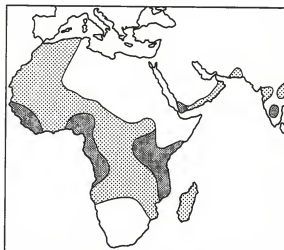
Heterozygotes and homozygotes

Individuals who are heterozygous (have nonmatching alleles) for sickle cell (Hb^A/Hb^S) are carriers of the condition but do not themselves suffer from the disease. It is only sickle-cell homozygotes (who have matching alleles - Hb^S/Hb^S) who have the condition. Individuals that are neither carriers nor sufferers are normal homozygotes (Hb^A/Hb^A).

Heterozygote advantage

- By natural selection, the sickle-cell allele (Hb^S) would be expected to be selected against until eventually none or very few remained in the population. Nevertheless, the allele sometimes remains at higher-than-expected levels.
- Furthermore, some parts of the world have much higher incidences of the sickle-cell trait than others.

The explanation appears to lie in the fact that being heterozygous for the sickle-cell allele is a positive benefit in those regions where a virulent form of malaria is present. As soon as the malaria-causing organism enters a red blood cell of a heterozygote, it causes the cell to sickle. The malarial parasite is unable to multiply in these sickled cells and so the progress of the disease is impeded. Unfortunately, similar protection is not offered to those who are homozygous for the sickle-cell condition. Nevertheless, the outcome is that heterozygotes have better survival rates



Frequency of sickle-cell allele:
 □ Below 1% ▨ 1-10%
 ■ 10-20%

than either of the homozygotes in those regions where a life-threatening form of malaria is prevalent. In such populations, the heterozygote is at an advantage and so the allele is retained at high levels.

Genotype	Heterozygote?	Name of genotype	Sickle-cell anemia sufferer?	Susceptibility to malaria
Hb^A/Hb^A	X	normal	X	average
Hb^A/Hb^S	✓	sickle-cell carrier	X	slight
Hb^S/Hb^S	X	sickle-cell anemia	✓	high

HYBRID VIGOR

The commercial production of plants – and, increasingly, of domesticated animals – involves the crossing of individuals from genetically distinct populations that have been inbred for desired characteristics. In plant breeding programs, different varieties or strains of the plant are crossed and the

resulting progeny, known as hybrids, have better characteristics than either of the parental strains. This is called hybrid vigor or heterosis. It arises because of the increased number of heterozygotes – individuals carrying nonmatching alleles (gene forms) – for particular genes.

1 Parental (P) generation

In this hypothetical example, the parents are two inbred strains of corn (a and b) homozygous (carrying matching alleles) for traits such as:

- growth (the alleles for which are indicated by A and a);
- resistance to disease (B and b);
- tolerance of herbicides (C and c); and
- abundance of corn cobs (D or d).

A, B, C, and D are dominant – expressed in preference to recessive (“weaker”) a, b, c, and d respectively. Each dominant allele gives the advantageous phenotype (expression) for its trait – fast growth; high resistance to disease; high tolerance of herbicides; and abundant corn cobs.

1

parents



P genotype

AAbbCCDD

P gametes

AbcD

b

P genotype

aaBBCCdd

P gametes

aBCd

2F₁ generationF₁ genotype

AaBbCcDd

3F₁F₂F₃F₄F₅F₆F₇F₈F₉F₁₀F₁₁F₁₂F₁₃F₁₄F₁₅F₁₆F₁₇F₁₈F₁₉F₂₀F₂₁F₂₂F₂₃F₂₄F₂₅F₂₆F₂₇F₂₈F₂₉F₃₀**1 parental strains****a****b**

FAST

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LOW

HIGH

LOW

HIGH

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Advantageous phenotype

Advantageous phenotype

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Advantageous phenotype

Advantageous phenotype

2 F₁ generation

FAST

SLOW

HIGH

HIGH

HIGH

MANY

FEW

Advantageous phenotype

Advantageous phenotype

Advantageous phenotype

Advantageous phenotype

Advantageous phenotype

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3 Subsequent generations

The F₁ hybrids are fertilized to produce the next (F₂) generation. The likelihood of recessive alleles being combined in homozygotes and therefore producing the disadvantageous phenotypes reappears. The accumulation of homozygous combinations explains why the inbred progeny of F₁ hybrids are less vigorous than their parents. The quality of plants continues to be reduced through each subsequent generation (F₃ on).

RING SPECIES

ALLOPATRIC SPECIATION

Speciation is the evolution of a new species. A ring species can evolve through a process of evolution called allopatric speciation. This refers to the evolution of two or more species from an ancestral species as a result of geographical separation. Allopatric speciation generally assumes that:

- complete geographical separation between evolving populations has occurred, and
- if they are brought back together again, the populations can no longer successfully interbreed.

This need not always be the case though:

- If discrete reproductive groups are in the

process of forming, and are not entirely separated geographically, there may be some interbreeding between them.

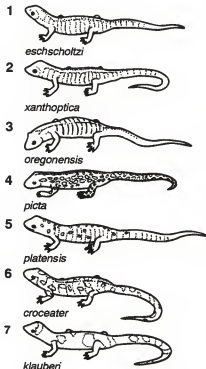
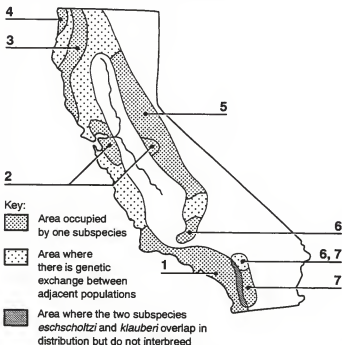
- If divergent selection pressure between such populations is strong and gene flow – exchange of gene forms (alleles) – between them is relatively weak, then this may give rise to a series of populations that are increasingly dissimilar.
- If the two populations at either end of the divergent series then come in contact, they may be sufficiently dissimilar to be unable to interbreed.

This has happened in certain instances and has given rise to ring species.

Example of a ring species

Populations of the salamander *Ensatina eschscholtzi* encircle California's central valley. The members of adjacent populations exhibit clear differences in body color and patterning. Hybrids do arise between adjacent populations, however. In some cases, there is extensive genetic exchange. The different populations are regarded as subspecies (or varieties) of the same species. The two southernmost populations (*Ensatina eschscholtzi* and *Ensatina eschscholtzi klauberi*) live in

the same territory but do not interbreed; they behave as two separate species. Were they not connected through the "ring" by a series of populations that exchange genes, then *klauberi* and *eschscholtzi* would be regarded as two separate species rather than as subspecies. They could be classed as separate species if one or more of the other subspecies within the ring were to become extinct and gene flow was permanently disrupted.



PUNCTUATED EQUILIBRIUM THEORY OF EVOLUTION

MACROEVOLUTION

The evolution of larger taxa (classification groups) than species – genera, families, orders, and so on right up to kingdoms – is called macroevolution. Until the early 1970s, the prevailing view was that macroevolutionary change took place gradually over many millions of years.

Macroevolution and the fossil record

- According to this view, the fossil record is expected to show the gradual evolution of species and larger classifications from preexisting species, as in the case of the evolution of the modern horse (see 7.08).
- Fossil sequences showing gradual evolution of new forms from existing ones are, however, comparatively rare.
- More usually, the fossil record shows long periods of stasis, when forms barely change, then the sudden appearance of new forms as if, in geological terms, they have appeared almost "overnight." This seems to contradict the view that evolution occurs by gradual change over millions of years.

There are two major explanations for this supposed contradiction:

- The fossil record is incomplete and the existing finds are too fragmentary to show the transitions in many fossil sequences. This view is upheld by those who believe evolution has occurred gradually.
- Another explanation is that speciation (the evolution of new species) occurs quickly and that there are long periods of stasis interspersed by periods of rapid evolutionary change. This is called the punctuated equilibrium theory of evolution. It was formulated by Niles Eldredge (born 1943) and Stephen Jay Gould (born 1941) in 1972.

Comparison of macroevolutionary models

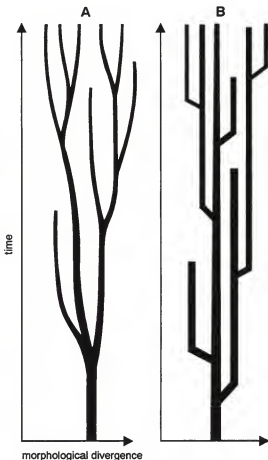
A The traditional, gradualist model of

evolutionary change sees new species arising slowly by gradual divergence from a common ancestor. The pace of evolutionary change is relatively constant.

B The punctuated equilibrium model sees

stasis as a normal part of evolution. Speciation is considered to happen only occasionally and in rapid bursts over relatively short periods of time – perhaps over 10,000 to 100,000 years rather than millions of years. During periods of stasis many species exist relatively unchanged (at least in body form) for perhaps 5–10 million years. The periods during which speciation occurs are thus very short in comparison.

Evidence for the two models Since 1972, paleontologists have been seeking fossil evidence to test whether the traditional view (gradualism) or the punctuated equilibrium model is correct. To date, there is no consensus of opinion. Some evidence supports the traditional view, and some (evolution of Lake Turkana snails in the east African Great Rift Valley, for example) supports the punctuated equilibrium model.



© DIAGRAM

SELFISHNESS, ALTRUISM, AND KIN SELECTION

Natural selection is a process by which organisms most suited to their environment become the ones most likely to survive and leave descendants. Populations evolve but it is individuals that are acted upon by natural selection. By the 1960s, biologists were taking this one stage further and were describing natural selection taking place at the level of the gene.

SELECTION OF GENES

Many aspects of animal form and behavior are difficult, if not impossible, to explain by natural selection acting on the individual. If the self-preservation of individual genes is taken into account, however, many puzzling observations can be explained.

Altruism

One of the thorniest problems for evolutionary biologists to explain is why some individuals in a population are altruistic (unselfish) – they are willing to die while protecting others.

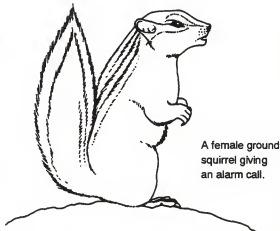
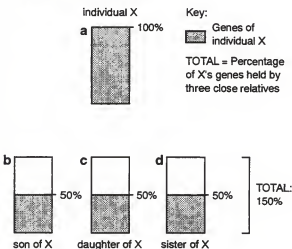
- If individuals are competing for food, territory, mates, and so on, why would they be willing to sacrifice themselves for the benefit of others?

The answer appears to lie in relatedness. An individual sacrificing itself is an adaptive advantage if, by doing so, it allows more of its own genes to survive. These genes will be present among related individuals. By doing a "cost-benefit analysis" (from the genes' point of view) of the relative advantages and disadvantages of such behavior, it is possible to see how altruistic strategies could have evolved.

Kin selection Related individuals have genes in common. On average, an individual (a) has 50% of its genes in common with a mother, father, son (b), daughter (c), or full brother or sister (d). If by sacrificing itself an animal can ensure the survival of at least three close relatives, a "cost-benefit" analysis reveals that for the loss of 100% of its own genes the animal could ensure the continued survival of 150% of its genes among close relatives. The evolution of such behavior in this manner is called kin selection.

An example of altruistic behavior Analyzed in this way, altruistic behavior ought to be more prevalent among those animals that live in closely-related groups, and this does appear to be generally the case. For example, North American ground squirrels live in colonies underground and when above ground an individual that senses danger will emit an alarm call that warns others but draws attention to itself. Females appear to give alarm calls more readily when in close proximity to relatives rather than nonrelatives.

An example of relatedness.



SOCIAL INSECTS AND KIN SELECTION

Related individuals have genes in common. It can be shown that animals are willing to sacrifice themselves if this will ensure the survival of enough their genes among close relatives. The evolution of such altruistic (unselfish) behavior in this manner is called kin selection.

Kin selection helps to explain the remarkable cooperation between social insects, which live in colonies:

- Many sterile workers can be found in the colonies of ants, bees, termites, and wasps.
- These workers labor for the benefit of the colony as a whole and yet, as they are sterile, they are unable to breed themselves.

This raises certain questions:

- Why do these individuals sacrifice their opportunities to reproduce?
- And how could this altruism have evolved on such a grand scale?

The advantages of this arrangement become clear when the genetic structure of a colony (honey bees, for example) is analyzed.

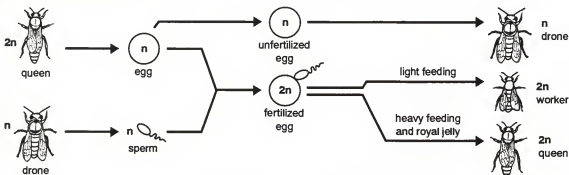
HONEY BEES

A colony of honey bees living in a hive is, in effect, one huge family. There are three main classes of honey bee in a hive:

- **The queen** is the only actively reproductive female present at any one time.
- **Workers** comprise the vast bulk of the colony. They are all sterile females.
- **Drones** are fertile males. They are present for a relatively short time. After fertilizing the queen they die.

Development of honey bees

All the honey bees in a hive develop from eggs laid by the queen:



Relatedness and kin selection among honey bees

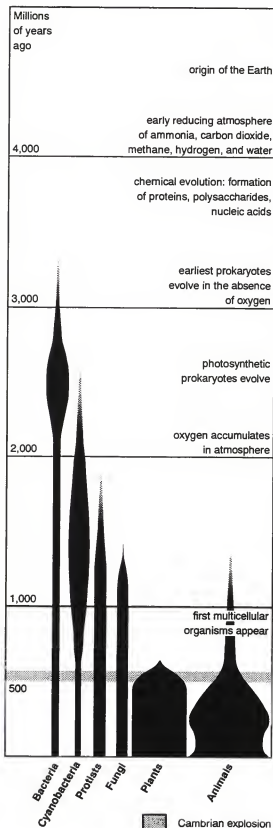
- **Drones**, being haploid, inherit all their genes from the queen. A male's relatedness to its mother is therefore 100%.
- **The queen's** relatedness to her male offspring, however, is only 50% – a drone has only half her genes.
- **Workers** derive half their genes from their mother, so their relatedness to the queen is 50%. Their relatedness to each other, however, averages 75% (they all inherit the same set of their father's genes and half of

their mother's genes). Viewed this way, a worker bee is more closely related to her sisters than to her mother. Other things being equal, the genes of a worker bee are more likely to be passed on, and in greater numbers, if she nurtures the queen (as a worker-producing factory) than were she to reproduce herself.

It is now possible to see how such a closely knit colony based on sterile workers might have arisen.

EVOLUTION OF LIFE

Current best estimates indicate that the Earth is about 4.6-billion-years old and for over three-quarters of that time (approaching 3.5 billion years) it has been inhabited by life forms.

**3.5–4 billion years ago**

- Chemical evolution in this period probably gave rise to macromolecules (large molecules) such as proteins, polysaccharides (complex sugars), and nucleic acids such as DNA (deoxyribonucleic acid). These came to form the building materials of the first and all subsequent living organisms.
- The first life forms were probably primitive bacteria. These early prokaryotes – organisms without a “true,” membrane-enclosed, nucleus (control center) – evolved in the oxygen-free environment.

2–2.5 billion years ago

- Photosynthesis – the ability of cells to use solar energy to create “food” from simple compounds – did not arise until about 2.5 billion years ago. This process liberated oxygen into the atmosphere.
- The atmosphere did not become oxygen-rich until about 500 million years later.

0.8–1 billion years ago

- Simple eukaryotic organisms (those that have a true nucleus) had probably arisen by this date.
- The primitive remains of multicellular forms have been found aged 850-million-years old.

500–570 million years ago

- As the planet cooled, and probably produced a greater diversity of habitats, a massive evolutionary diversification occurred called the Cambrian “explosion.” By the end of the Cambrian Period some 500 million years ago, nearly all the major animal phyla (classification groups) had been established.

Since 500 million years ago

- First invertebrates (animals without backbones) and then vertebrates (animals with backbones) colonized the land.
- Five major extinctions have occurred: in the late Ordovician; late Devonian; end-Permian; end-Triassic; and end-Cretaceous. Various explanations have been suggested for these mass extinctions. For example, the end-Cretaceous extinction event (which saw the demise of the dinosaurs) may have been caused by one or more meteorite impacts that ejected debris into the atmosphere and triggered a rapid climatic change.

100,000 years ago to the present day

- Modern humans (*Homo sapiens sapiens*) had evolved by 100,000 years ago.
- The extinctions being perpetrated by human activities (some estimates give 30,000 species being lost each year) suggest that the planet is currently undergoing a mass extinction event that may, within centuries, wipe out entire taxa of animals and plants.

COEVOLUTION

Coevolution is a general term that refers to the evolution of one species in response to changes in an unrelated species.

Coevolution in animals

The "arms" race between predators and their prey is a form of coevolution. As prey species (zebra, for example) evolve to become better at escaping predators (such as lions), the predators must adapt accordingly if they are to survive by preying on that species. They must run faster, have more powerful claws, jaws, and teeth if they are to catch and hold their prey. In turn, prey species evolve better strategies for evading their predators.

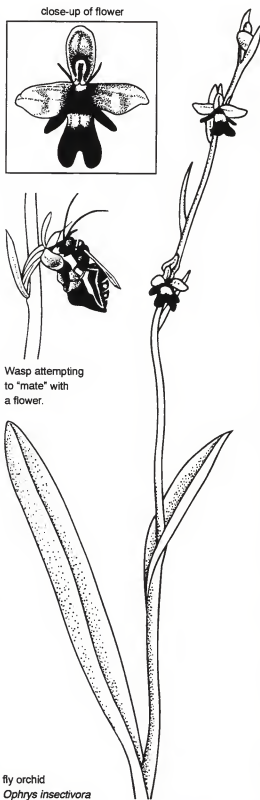
Coevolution in plants and insects

Flowering plants evolved on land after insects were already well established. These plants have since evolved to utilize insects as an efficient means of ensuring cross-pollination:

- Flowers have evolved to be visually attractive to insects.
- Also, many produce sugar-rich nectar to entice insects to feed and so carry pollen grains from one flower to another.
- To help ensure that an insect pollinates flowers of the same plant species, the flowers are generally easy to distinguish, bloom at a specific time of the year, and contain only small amounts of nectar so ensuring that the insect visits many flowers.

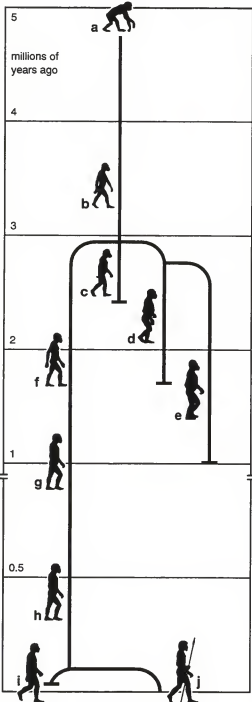
Although most relationships between a plant and its insect pollinator are mutually beneficial, some plants have taken this a step further and are able to attract insects without providing a reward:

- Many orchids, for example, have developed flowers that resemble the abdomen of a female wasp or bee of a specific species.
- The flowers also exude chemicals that resemble the fragrance of the female insect.
- Males of the species are attracted to the orchid's flowers and attempt to mate with the flower.
- In this way, they pick up pollen that is then transferred to another flower of the same species when they "mate" again.
- Although the wasp or bee appears to gain no benefit from this relationship, the flower's strategy does not appear to seriously affect the insect's ability to mate successfully – if it did, insect numbers would fall and this, in turn, would affect the flower's ability to cross-pollinate.



HUMAN EVOLUTION

Human evolution is perhaps the fastest changing area of evolutionary research. Year by year new discoveries are radically changing opinions about the origins of humankind – our nearest ancestors, geographic origins, and the evolutionary timescale. The scheme shown here is just one of several proposed in recent years.



The evidence for human origins comes from several approaches:

- The traditional, and still important, approach involves analysis of fossil remains and associated artifacts coupled with sophisticated dating techniques.
- Increasingly, molecular biological techniques have been used to establish the degree of genetic similarity between humans and their primate relatives, and also between different ethnic groups to establish patterns of migration for human populations within the last 100,000 years.

Current evidence suggests:

- The evolutionary branch leading to humans diverged from that leading to the chimpanzees (our closest living primate relatives) about 5–7 million years ago.
- The first hominids that showed evidence of bipedalism – habitually walking on two legs – were the australopithecines of which there are at least two recognized species. Hominids are members of the *Hominidae* family, which includes the gorilla and the chimpanzee as well as the ancestors of humans.
- *Homo erectus* appears to have been replaced by an "archaic" form of our species, *Homo sapiens*, which evolved in the last half a million years. *Homo sapiens* gave rise, in the last 100,000 years or so, to two subspecies, *Homo sapiens sapiens* (modern humans) and *Homo sapiens neanderthalensis* ("Neanderthal man"). The latter died out some 30,000–40,000 years ago.

- | | |
|--------------------------------|-------------------------------|
| a <i>Ramapithecus</i> | e <i>Paranthropus boisei</i> |
| b <i>Australopithecus</i> | f <i>Homo habilis</i> |
| afarensis | g <i>Homo erectus</i> |
| c <i>Australopithecus</i> | h <i>Homo sapiens</i> |
| affricanus | i <i>Homo sapiens</i> |
| d <i>Paranthropus robustus</i> | neanderthalensis |
| | j <i>Homo sapiens sapiens</i> |

One of the major trends in human evolution has been an increase in cranial capacity – an increase in brain size as indicated by the size of the cranial space within the skull. Increasing brain size, in the case of human evolution, is interpreted as being associated with increasing intelligence, more complex social behavior, tool-making, and an increased use of language.

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